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REVIEW ARTICLE

# Traditional, complementary and alternative medicine in children constipation: a systematic review

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## Abstract

**Objectives** This review aims to evaluate the efficacy and safety of complementary and alternative medicine methods for constipation in the pediatric population.

**Evidence acquisition** Medical literature search was performed in several databases for a variety of Traditional, Complementary and Alternative Medicine in childhood constipation. Databases included Web of Science, Scopus, Embase, Cochrane Library, PubMed, ScienceDirect, Google scholar and a number of Persian databases including IranDoc, Magiran and SID. No time limitation was determined. Clinical trials or case series that had evaluated the effectiveness of CAM therapies in functional constipation of 1–18 year old children were included. Papers not in English or Persian language were excluded. Related articles were screened independently by two reviewers according to their titles and abstracts. A data extraction form was filled in for each eligible paper. Quality assessment of eligible documents was also performed.

**Results** 30 studies were included, comprising 27 clinical trials and 3 case series. Ten documents were on herbal medicine, nine on traditional medicine, ten on manual therapies and one on homeopathy. Except for two herbal and one reflexology interventions, all studies reported positive effects on childhood constipation, with the majority being statistically significant. As the number of studies in each method was limited, we could not perform a meta-analysis.

**Conclusion** The scarcity of research on the efficacy and safety of different types of complementary and alternative medicine methods in children with constipation necessitates conducting more studies in each field.

**Keywords** Complementary therapies · Alternative medicine · Traditional medicine · CAM · Constipation · Pediatrics

## Objectives

Although initially a benign condition, functional constipation in the pediatric population is an important issue in healthcare systems [1]. The prevalence of childhood constipation varies in different countries, ranging from 0.7% to 29.6% [2]. Approximately 30.8% of 2 to 12 year old Indian children are affected by this condition [3]. In Colombia, the prevalence is

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14.5% in children aged 8 to 12 years and 10% in 13 to 18 year olds [4]. In china, 18.8% of the pediatric population suffer from constipation in contrast to 8.2% in the general population [5]. Moreover, 3% of all general pediatric visits and up to 25% of visits by pediatric gastroenterologists in the USA are attributed to constipation [6].

The economic burden of constipation in the pediatric population is also variously reported [7]. The mean total unadjusted annual expenditure for children with constipation is 3 times higher than those not affected by this condition [8]. Furthermore, some disorders such as headache, depression, anxiety, influenza, otitis media, and asthma are more prevalent in constipated children, resulting in extra costs for healthcare systems [9]. In 2011, the number of 1–17-year-old children with constipation visited in USA emergency wards was 50.7% more than similar population in 2006. This increase can be attributed to a sedentary lifestyle, obesity, and increased use of medications in the recent years [10]. Accordingly, more burden can be expected in the future years. Constipation obviously affects a child's quality of life. This is demonstrated by lower scores in quality of life tests compared to healthy children. Their scores are even significantly less than those affected by GERD and IBD [11]. Drawing attention to the chronicity of the condition, it has been demonstrated that only 60% of children are symptom free 6–12 months following initiation of treatment [12]. In longer follow-ups, symptoms remained in one out of four children, in some instances even persisting into adulthood [13].

Considering the mentioned condition altogether, it is anticipated that some parents seek alternative or complementary treatments hoping for probable better outcomes. Lifetime usage of complementary and alternative therapies for children and adolescent varies from 10.9% to 87.6% in different countries, with the current rate being 0.8% to 48.5% [14]. In Germany, 26% of used remedies are CAM remedies [15]. In gastroenterology clinics of the Netherlands, CAM usage rate is 25.3% for functional and 17.2% for organic gastrointestinal problems. Among children with constipation, approximately 36.4% use CAM therapies for various conditions, while 24.1% use them to treat their constipation. While 93% of the parents believed in the necessity of clinical research on CAM, 51% declared that they would consent to their child participating in such studies [16].

Beyond parent viewpoints, evaluating the effectiveness and safety of CAM modalities in children is a realistic and even urgent need that should be prioritized in more prevalent diseases and those that cause more burden.

This review aims to evaluate the efficacy and safety of a variety of complementary and alternative medicine subtypes in childhood constipation.

## Evidence acquisition

### Data sources

Medical literature search was performed in databases including: Web of Science, Scopus, Embase, Cochrane Library, PubMed, ScienceDirect, Google scholar and some Persian databases including IranDoc, Magiran and SID to May 2019. All databases were searched without time limitation. Only English or Persian papers were included.

### Study selection

The search strategy was: constipation[Mesh Terms and free text terms] AND (pediatrics [Mesh Terms and free text terms] OR pediatric [Mesh Terms and free text terms] OR child[Mesh Terms and free text terms]) AND (Acupuncture OR acupressure OR "Guided imagery" OR "Alexander technique" OR Hypnosis OR Massage OR Meditation OR Reflexology OR Rolfing OR "structural integration" OR "Tai chi" OR "Therapeutic touch" OR "Ayurvedic Medicine" OR Ayurveda OR "Siddha Medicine" OR Yoga OR Curanderismo OR "Native American Medicine" OR TCM OR "Traditional Chinese Medicine" OR "Persian Medicine" OR "Traditional Iranian Medicine" OR "Iranian Traditional Medicine" OR "Tibetan Medicine" OR "Unani Medicine" OR "Anthroposophic Medicine" OR Chiropractic OR Homeopathy OR Naturopathy OR Osteopathy OR herbal OR phytomedicine OR phytotherapy).

Related papers were screened according to their titles and abstracts. Papers with uncertain decisions were studied thoroughly. Every paper was independently studied by two of the three reviewers (MSP, MSM and SB). In case of disagreement, reviewers made a decision after discussing the issue. Otherwise the third reviewer would assist. Bibliography of papers were searched to find cross references.

### Eligibility criteria

Eligibility criteria included 1) clinical trials or case series evaluating the effectiveness of CAM therapies in functional constipation in children; 2) study population in the age range of 1–18; 3) the study being on one of the aforementioned CAM methods; 4) language of evidence being English or Persian.

### Data extraction

A data extraction form was designed to obtain necessary information of the documents such as age of participants, details of interventions, diagnostic criteria for constipation, tools used to follow up patients, criteria used to define response, methodological factors and primary and secondary outcomes of the study. Each document was reviewed by two of three reviewers

(MSP, MSM and SB) independently. In case of different opinions that could not be resolved by discussion, the third reviewer would help. If information was not sufficient, further information was obtained from the corresponding author via email.

### Quality assessment

JADAD score [17] was used to assess the quality of clinical trials. The quality of case series studies was evaluated by CARE extensions for homeopathic and therapeutic massage and bodywork [18, 19]. Two of the three reviewers performed the quality assessments of every paper according to the aforementioned procedure.

## Results

A total of 6993 studies were retrieved. 3995 studies were excluded because they were not English/Persian or were duplicate; consequently, 2998 studies were screened according to their titles and abstracts.132 records were studied thoroughly to assess their eligibility. Their reference lists were screened to find more related studies other than those that were found in electronic searches, but no additional study was found. Finally, 30 records were included. The process is summarized in a flow diagram in Fig. 1. Detailed information of these 30 studies are summarized in Table 1.

## Characteristics of included studies

Filho et al. [49] reported the effect of homeopathic interventions on a variety of different patients. A group of constipated children was among the cases, and so we extracted a case series of the effectiveness of homeopathy in childhood constipation. In the study conducted by Iwai et al., 15 constipated patients were enrolled, five of which had a history of anorectal malformations and were thus excluded. The remaining ten patients were included in our study.

## Description of included populations

Six studies included patients with disabilities. Although these conditions can influence constipation, we decided not to exclude them, due to the scarcity of studies about such interventions in otherwise healthy children. Two studies were performed on CP patients, two on mentally disabled, and one in patients with tertiary healthcare needs. In one study (Day et al.) the characteristics of patients are mentioned as disability in brief. These disabilities can be explained as Down syndrome, hemiplegia, Rette syndrome, and etc.

In a study by Cai, 478 patients were allocated to intervention and placebo groups in a ratio of 3:1 to ensure statistical significance and consider the research grant.

## Classification of interventions

We categorized included studies under four categories: herbal medicines, traditional medicines, manipulations and other.

### Herbal medicines

Ten studies had assessed herbal interventions in children constipation.

Some herbal medicines are a compound of different plants. Fruitlax is a blend of raisin, currant, prune, fig and date. AFPFF is the mixture of acacia fiber, psyllium fiber, and fructose. Fijan Figs is a syrup containing fig and senna extract.

Glucomannan is a fiber gel polysaccharide derived from Japanese Konjac tubers. Its efficacy on childhood constipation was assessed in three studies.

PHGG is obtained from guar gum, a water-soluble fiber from seeds of *Cyamopsis tetragonoloba*. It has a smaller molecular weight and less viscosity than guar gum [23].

Black strap molasses and red sugar are byproducts in the sugar-making process. Sugar syrup (molasses) is what causes the color of red sugar. They are both derived from *Saccharum officinarum* (sugarcane) [35, 36].

### Traditional medicines

According to WHO, Traditional medicine is “the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness” [50].

Dai-Kenchu-To is a traditional Japanese preparation that is a combination of zanthoxylum fruit, ginseng root and dried ginger rhizomes.

Xiao’er Biantong (XEBT) is a drug from Traditional Chinese Medicine. It is the first Chinese patent medicine for functional constipation in children and is composed of seven herbs.

Mozaffarpur et al. Nimrouzi et al. and Esmaeilidooki et al. had designed their studies based on Persian Medicine, as well as Shahamat et al. that has studied the efficacy of dry cupping on childhood constipation. Cupping is performed by placing a cup on the skin and applying negative pressure by suction [34, 51] .

The study by Mali was designed according to Ayurveda, one of the traditional medicinal systems of India.

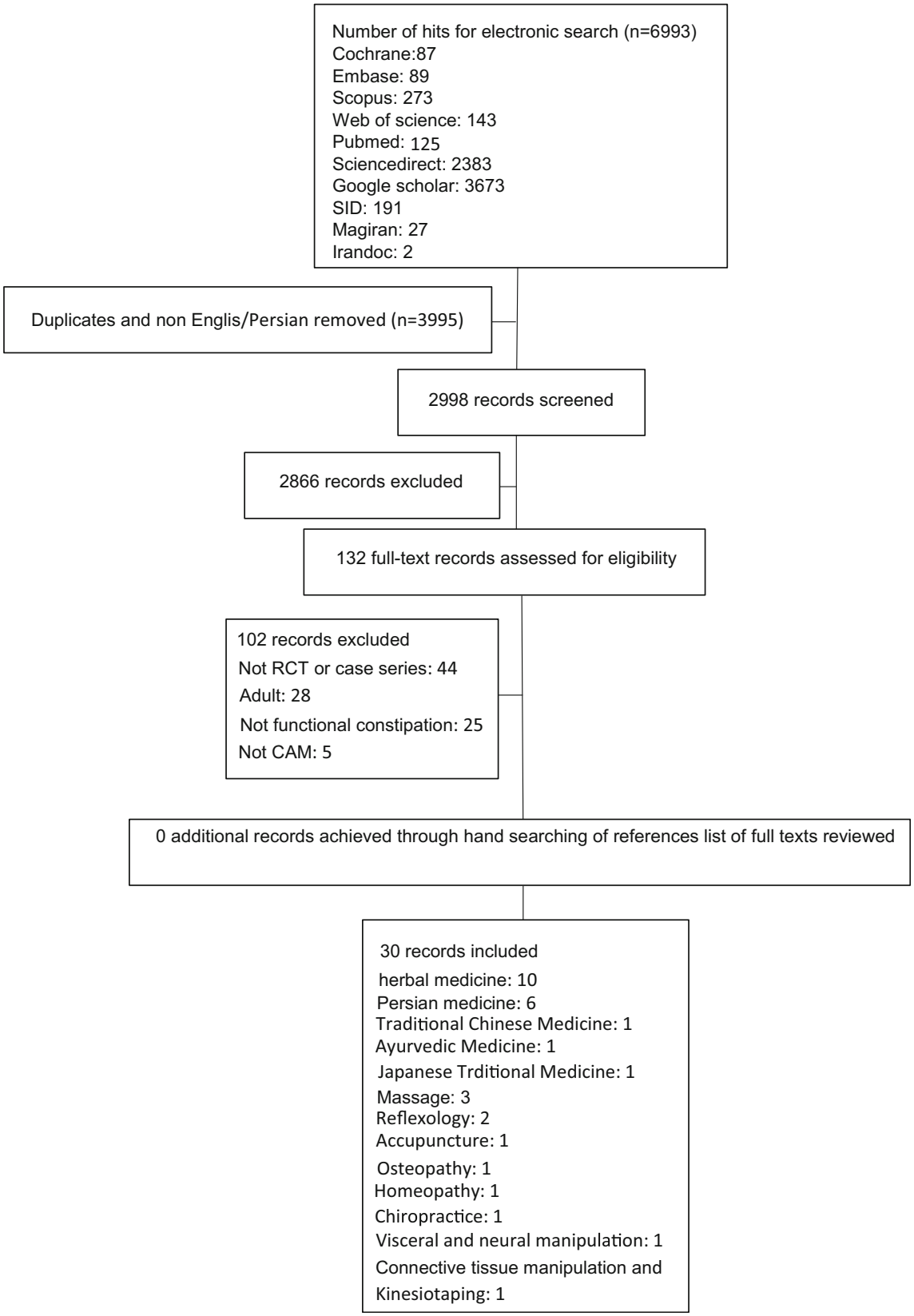


**Fig. 1** Flow diagram of assessment of identified studies

**Table 1** Characteristics of included studies

| | First author (year) | Study design | Total sample (female patients) other characteristics | Age in year | Diagnostic criteria | Criteria used to define response |
|---|---|---|---|---|---|---|
| Herbal Medicine | Day [20] (1995) | Quasi experimental, single subject, AB design | 7 (5) Disability | 3–9 | Identified by a parent and a healthcare worker | Improvement of frequency/ amount/ color/ consistency of stool; defecation effort; need for medication to relieve constipation |
| | Loening-Baucke [21] (2004) | Double blind crossover RCT | 31 (15) | 4.5–11.7 | Delay or difficulty in defecation, for 2 w, causes significant distress | DF/W > =3 and SE/3 w < =1 with no abdominal pain |
| | Castillejo [22] (2006) | Double blind RCT | 56 (34) | 3–10 | Rome II | CTT |
| | Ustundag [23] (2010) | RCT | 61 (−) | 4–16 | Rome III | Soft to formed stool; no pain/ stool withholding /blood in stool/ palpable rectal or abdominal mass |
| | Chmielewska [24] (2011) | Double blind RCT | 80 (46) | 3–16 | Rome III | > = 3 Stools/w with no soiling |
| | Quitadamo [25] (2012) | RCT | 100 (62) | 4–10 | Rome III | ≥3 bowel movements/w, ≥2 stool consistency grade on BSFS, no fecal incontinence, abdominal pain, pain on defecation or fecal bleeding. |
| | Horvath [26] (2013) | Follow up of Chmielewska, et al | 63 of 72 | 3–16 | A standardized questionnaire | DF > =3, no SE in last week, abdominal pain, or need for laxatives |
| | Staiano [27] (1999) | Double blind RCT | 19 (5) severe brain damage | 5.7 ± 4.2 y | An arbitrary scoring system | Stool habits, total and segmental gastrointestinal transit times, and anorectal motility |
| | PerKin [28] (1977) | Crossover RCT | 21 | Under 15 | > = 3 months of History of constipation | Improvement in number and characteristics of stools |
| | Closa-Monasterolo [29] (2017) | Double blind RCT | 17 (9) | 2–5 | Rome III | Improvement in symptoms of constipation and stool characteristics |
| Traditional Medicine | Iwai [30] (2007) | CT | 10* Severe constipation | 6–13 | Clinical scoring system by JSGA | Clinical scoring system by JSGA, anorectal manometry |
| | Mozaffarpur [31] (2012) | RCT | 81 (29) | 4–13 | Rome III | <=2 criteria from Rome III |
| | Nimrouzi [32] (2015) | RCT | 109 (61) | 2–12 | Rome III | DF > =3, soft stool, convenient defecation, no SE and bloody stool/w, exiting the Rome III |
| | Esmaeilidooki [33] (2016) | Open label RCT | 109 (46) | 2–15 | Rome III | To exit from Rome III |
| | Shahamat [34] (2016) | RCT | 120 (52) | 4–18 | Rome III | DF > =3, soft stool, convenient defecation, no soiling or bloody stool, not fulfilling Rome III for constipation |
| | Tajik [35] (2018) | RCT | 60 (20) | 2–10 | Physician decision | Improvement in a designed questionnaire |
| | Dehghan [36] (2019) | Double blind RCT | 92 | 4–12 | Rome III | Improvement in DF, absence of lumpy or hard stools, abdominal pain and retention, soiling and blood-stained stool, sensation of anorectal obstruction/ blockage |
| | Mali [37] (2016) | Single blind CT | 10 (−) | 2–8 | Hard stool | An assessment criteria** |
| | Cai [38] (2018) | Double blind RCT | 478*** (251) | 1–14 | Rome IV | Improvement of median effectual time of defecation, main symptom score and disappearance rate of symptoms and the differences between groups |
| Manipulations | Broide [39] (2001) | CT | 32 (10) | 2–14 | A bowel habit questionnaire | Increase of DF |

**Table 1** (continued)

| | First author (year) | Study design | Total sample (female patients) other characteristics | Age in year | Diagnostic criteria | Criteria used to define response |
|---|---|---|---|---|---|---|
| | Gordon [40] (2007) | Single blind RCT | 176 (81) | 1–12 | Rome II | Mean increase of 4.5 complete bowel movements per week in 4 weeks |
| | Alcantara [41] (2008) | Case series | 3 (2) | 21,7,21 m | – | Improved bowel movements |
| | Tarsuslu [42] (2009) | CT (Pilot study) | 13 (5) CP | 2–16 | CAS | CAS, VAS, DF |
| | Silva [43] (2013) | Triple blind RCT | 72 (42) tertiary healthcare needs | 4–18 | Rome III | – |
| | Bromley [44] (2014) | CT | 25 (–) Mental disability | 3 m- 19 y | NICE (2010a & 2014) | – |
| | Orhan [45] (2016) | RCT | 45 (19) CP | 4–18 (4.5–1-1.5) | Rome III | VAS, PEDsQL, BSFS and 7-day bowel diaries |
| | Elbasan [46] (2018) | RCT | 40 (16) CP | 3–15 | Modified Constipation Assessment Scale (MCAS) | Modified Constipation Assessment Scale (MCAS) |
| | Canbulat Sahiner [47] (2017) | RCT | 40 | 3–6 | Rome III | Defecation number and consistency |
| | Zollars [48] (2018) | Case series | 5 (2) CP | 3–18 | Rome II criteria modified for children with cerebral palsy | Improvement in radiographically assessed colonic motility, DF or quality of stool |
| Others | Filho [49] (2005) | Case series | 5 (3) Mental disability | 1–7 | Patient complaint (3), homeopath diagnosis (2) | An improvement scale |

| | Experimental intervention | Control intervention | Follow up (s) | Primary outcome measures | Main results |
|---|---|---|---|---|---|
| Herbal Medicine | Fruitlax<br>18 m-6y:4 ts/d, if stool still hard on 3rd day, increased daily until stool became soft (max: 7 ts/d)<br>scales for 6–12 y and > 12 y were also developed | No control group | Baseline A (2 w), intervention period B (> = 3 w) | Frequency/ amount/ color/ consistency of stool; defecation effort; need for medication to relieve constipation. | Each child experienced individual changes in bowel pattern |
| | 4 w glucomannan and 4 w placebo, both 100 mg/kg (maximum of5 g/d) | | 4th, 8th w | DF, soiling frequency, and disappearance of abdominal pain in the last 3 weeks of a 4-week treatment | Glucomannan is beneficial in childhood constipation ± encopresis |
| | Cocoa husk supplement sachet (containing 4 g of cocoa husk)<br>3–6 y: 1<br>7–10 y: 2<br>before lunch and dinner +<br>standardized toilet training procedures | Placebo +<br>standardized toilet training procedures | 4th w | CTT | Significant differences between groups when total basal intestinal transit time was in the 50th percentile |
| | PHGG in fruit juice during or between meals<br>4–6 y: 3 g/d; 6–12 y: 4 g/d; 12–16 y: 5 g/d | lactulose (1 ml/kg/d, in divided doses) | 4th w | ND | No statistical difference between groups ($P > 0.05$) |
| | Glucomannan 2.52 g/d | Placebo (maltodextrine) 2.52 g/d | 4th w | Treatment success (> = 3 stools/w with no soiling) | Treatment success was similar in both groups (relative risk 0.95, 95% CI 0.6 to 1.4) |
| | AFPFF<br>16.8 g daily (up to 22.4 g, while not improved after at least 3 d of treatment) | PEG 3350 with electrolytes (PEG+ E)<br>(0.5 g/kg daily) | 1st, 2nd, 4th, 8th w | Improvement of constipation | 77.8% of AFPFF group and 83% of PEG+E group improved ($P = .788$) |
| | – | – | | Treatment success | |

**Table 1** (continued)

| | Experimental intervention | Control intervention | Follow up (s) | Primary outcome measures | Main results |
|---|---|---|---|---|---|
| | | | 24 m after completion of previous study | | Treatment success in 57%, functional constipation in 27%, need for laxatives 21% no differences between groups |
| | Glucomannan 100 mg/kg BD | Placebo | 4th, 8th, 12th w | Number of bowel movements per week, stool consistency, presence of painful defecation, abdominal distention, use of laxative or suppository | Glucomannan significantly increased stool frequency (P < .01), decreased painful defecation per week (*P* < .01) And improved stool consistency |
| | Lactulose (10–15 ml daily) or Senna syrup (10–20 ml daily) in 1st w, no treatment in 2nd w, the alternative treatment in 3rd w | | Beginning of 2nd and 3rd w | Number of patients passing stools of any kind each day | Significant difference, in favor of lactulose, in the number of days on which normal stools were passed during the treatment weeks |
| | Orafti® inulin-type fructans 2 g BD, mixed into a non-pre or probiotics dairy product | Placebo (maltodextrin) 2 g BD, mixed into a non-pre or probiotics dairy product | 6th w | Stool consistency | Stool consistency improved from 2.2 to 2.6 on the modified Bristol scale for children in intervention group ($p = 0.040$). no improvement in control group |
| Traditional Medicine | 0.3 g/kg/d of DKT ,from 3 m to 1 y duration | No control group | Before and after intervention | Clinical score for bowel function, manometric study | DKT improved clinical score for bowel function (*P* < 0.02), threshold sensation volume and rectal compliance (*P* < 0.05) and maximum tolerable volume (*P* < 0.01) |
| | CFE, 0.1 g/kg in three-separated doses (after each meal) | Mineral oil: 1 ml/kg/d | 1st, 2nd, 3rd w | Improvement in 1) DF, 2) fecal incontinence episodes, 3) retentive posturing episodes, 4)average of severity of defecation pain (by VAS) 5)average of consistency of stool (by VAS) per week | DF was higher in CFE group (P < 0.001), severity of pain during defecation and consistency of stool were better in CFE group (P < 0.05) |
| | Oral solution of *Descurainia sophia L.* seeds 2–4 y: 2 g/d 4–12 y: 3 g/d for 8 w | PEG 40% without electrolyte (0.4 g/kg) | Weekly | Proportion of patients who had responded to treatment | No significant difference between groups in DF, Hard stool, Painful defecation and soiling |
| | 1 cc/kg /d of CFE in 3 divided doses, for 4 w | 0.7–0.8 g/kg/d of water soluble PEG twice daily | 1st, 2nd, 3rd,4th w | DF, consistency of stools, severity of pain during defecation, retentive posturing and fecal incontinence per week. | All measures improved in both groups. no significant difference, except for DF that was significantly more in CFE group |

**Table 1** (continued)

| | Experimental intervention | Control intervention | Follow up (s) | Primary outcome measures | Main results |
|---|---|---|---|---|---|
| | Dry cupping, fourteen 8 min sessions, 4–6 cups, 1.5–5 cm in diameter (10–100 cc), every other day | PEG (40% solution without electrolyte), 0.4 g/kg once daily | 2nd, 4th, 8th, 12th w | Improvement of constipation | than PEG group ($P < 0.0001$)<br>decreased constipation in PEG group ($P < 0.01$) at 2nd and in cupping group (P= 0.03)<br>at 4th w<br>no significant difference at 8th and 12th w |
| | Red sugar powder<br>2 g / kg / day | Fijan (containing figs and senna extract)<br>2 cc / kg / day | 2nd, 4th w | Functional characteristics of constipation such as DF | Red sugar was more effective in reducing anorexia and abdominal pain ($p < 0.001$);<br>No significant difference between groups in DF and pain during fecal excretion |
| | BSM (black strap molasses)<br>1 mL/kg daily for 1 month. | PEG syrup | 2nd, 4th w | Improvement in DF, absence of lumpy or hard stools, abdominal pain and retention, soiling and blood-stained stool, sensation of anorectal obstruction/ blockage | Significantly improvement of DF in both groups; Decreased volitional stool retention, large diameter stool, painful or hard stool and large fecal mass in the rectum ($P < 0.05$); no significant difference between groups except for the rate of large diameter stool |
| | Haritaki Churna (*Terminalia chebula*) + Madhu (honey), 0.7 - 2 g/d (acc. to Dilling formula) BD + Dietary advices | No control group | 5th d | Improvement of constipation | Constipation improvement ($P < 0.001$) |
| | Xiao'er Biantong (XEBT) granules<br>1–3 y: 2.5 g, TDS<br>4–6 y: 5 g, BD;<br>>7 y: 5 g, BD | Placebo granules<br>1–3 y: 2.5 g, TDS<br>4–6 y: 5 g, BD;<br>>7 y: 5 g, BD | 1st, 2nd, 4th w | Frequency of spontaneous bowel movements (SBM) for 14 days | SBM for 14 days were 8.89 in XEBT group and 5.63 in placebo group ($p = 0.0001$) |
| Manipulations | 5 weeks of placebo followed by 10 weeks of true acupuncture up to<br>3 needles for 20 min | Healthy controls received no treatment | After 5, 10, 15 acupuncture session | DF and panopioid activity | DF↑ ($P < 0.001$)<br>panopioid activity↑ ($P < 0.001$) |
| | Group 1: Reflexology Group 2: Foot massage, both by parents/care givers + conventional treatment in both | Standard treatment | 12th, 24th, 36th w | Number of complete bowel movements in 4 weeks period | In the 12th w, the reflexology group experienced the greatest reduction in total constipation score 9.91 (SD 8.153)<br>95% CI 7.87–11.94 compared to 13.91 (SD11.491) 95% CI 10.86–16.96 in control<br>and 13.67 (SD 10.120) 95% CI 10.94–16.41 in massage group ($p = 0.047$) |
| | Full spine chiropractic care (high velocity low amplitude thrusts and the activator technique) 3 w to 3 m | – | 1–3 y follow up | Bowel movement | Normal bowel movements in all patients |

**Table 1** (continued)

| | Experimental intervention | Control intervention | Follow up (s) | Primary outcome measures | Main results |
|---|---|---|---|---|---|
| | Osteopathy:<br>fascial release, iliopsoas<br>muscle release, sphincter release, and bowel mobilizations<br>during 30<br>minutes, 3 /w for 6 m | Osteopathy+ lactulose<br>)initiated 10 mL/d for children <6 y, 15 mL/d for children older. After 1 w, doses were<br>halved | 3rd, 6th m | CAS, VAS, DF | CAS↓ (P < .05), constipation improvement (*P* < .05) in both groups.<br>No difference between groups in either<br>aspects (*P* > .05) |
| | Abdominal muscle training+ breathing exercises+ abdominal massage<br>40 min × 2 sessions /w<br>+ control group interventions | Magnesium hydroxide at least 2 mg/kg PRN + fiber dietary<br>foods, water and toilet training | 6th w | DF and retentive fecal incontinence | Higher DF in physiotherapy group than in medication<br>group (*P* = 0.01) |
| | Abdominal massage by parents, 20 min/d<br>(as preferred e.g., 5 min × 4 or 10 min × 2) | No control group | 6th w | Constipation improvement | Improved quality of life (100%), symptom relief<br>(87.5%), reduced laxative use (58%),<br>improved dietary intake (41%). |
| | CTM:<br>Three 15–20 min sessions/w + lifestyle advice.<br>lower thoracic, scapular, inter-scapular and cervical regions<br>KT: 3/w + lifestyle advice | Lifestyle advice | 4 w | DF | Among the CTM, KT, and control groups, there were statistically significant differences regarding<br>the changes in DF (2.46, 3.00, 0.30, ES 1.16, P < 0.001), |
| | Foot reflexology, 20 min sessions, twice a week for 8 weeks + neurodevelopmental therapy | Neurodevelopmental treatment program, 45–60 min sessions, twice a week, for 8 weeks. | 8th w | MCAS score | Decrease in MCAS scores in reflexology<br>group (<0.001)<br>no significant difference between groups |
| | Foot massage with baby oil<br>(10 min × 5 / w)<br>toilet/diet/<br>motivation training for parents<br>(30 min, once per week) | Toilet/diet/motivation training for parents (30 min, once per week) | 1st, 2nd, 3rd, 4th w | Stool number and consistency | No significant differences in stool frequency and consistency between groups (p > .05) |
| | Visceral and neural manipulation focused on abdomen and related aspects of the nervous system, 45 min sessions, every 2 w for a total of 24 w | – | 8th, 16th, 24th and 36th w | Radiographically assessed colonic motility, DF and quality of stool | Number of bowel movements increased<br>during the study for all participants |
| Others | Individually according to homeopath decision | – | Individually | Improvement of constipation | 2 cases: clear improvement,<br>1 case: partial improvement,<br>2 cases: no changes |

*AFPFF* a mixture of acacia fiber, psyllium fiber, and fructose, *BSFS* Bristol Stool Scale, *CAS* Constipation Assessment Scale, 2006, *CFE Cassia fistula* emulsion, *CT* Clinical Trial, *CTM* Connective Tissue Manipulation, *CTT* Colonic Transit Time, *d* day/ days, *DF* defecation frequency (times/week) *DKT* Dai-Kenchu-To, *ES* Effect Size, *JSGA* Japanese Study Group of Anorectal Anomalies, *KT* Kinesio Taping, *m* month/ months, *ND* No Declaration, *NICE* National Institute for Health and Care Excellence, *PEDsQL* Pediatric Quality of Life Questionnaire, *PEG* Poly Ethylene Glycol, *PHGG* partially hydrolyzed guar gum, *RCT* Randomized Controlled Trial, *SE* Soiling Episode, *Ts* teaspoon, *VAS* Visual Analogue Scale (VAS), *w* week/ weeks, *y* year/years

*Five children with constipation after surgery for anorectal malformations were excluded from the study

**Vibandha (difficult stool pass)

1 Normal: 00

2 Alpasha, Grathita Malapravrutti: 01

3 Avashthambhit Malapravrutti: 02

***359 patients in intervention and 119 patients in control group

### Manipulations

Ten studies evaluated the effects of manual techniques on constipation in children. Some definitions are provided in the following.

Reflexology: application of specific massage technique on hands, feet and ears believed to impress function of organs. [46].
Osteopathy: hands on techniques used to rectify and regulate structural and functional systems by careful examination of the tonus and texture of tissues and correction of restrictions and abnormal movements consequently [42].
Chiropractic: the conservative management of neuromusculoskeletal system with special emphasis on the spine [52, 53].
Visceral and neural manipulation focuses on fascia, nerves, bones, joints, body organs and the vasculature. Visceral manipulation is a hands-on method that involved in normal mobility, tone, and tissue motion of the viscera and their connective tissues attachments. Neural Manipulation is a manual therapy that recognizes and treats neural and dural restrictions in association with cranium and spinal hard frame [48].
Connective Tissue Manipulation: a manual therapy that stimulates segmental and supra-segmental cutaneo-visceral reflexes, which can retrieve autonomic balance and result in better functioning of organs [45].
Kinesio Taping: In Kinesio Taping, elastic, latex-free, adhesive and thin bands are used. They can be stretched up to between 40% and 60% of its original length, similar to the elasticity of the skin [45].

It seems that in the recent years, more trials are being carried out on the efficacy of various manipulations on constipation in the pediatric population.

No clinical trials or case series were found in fields of Alexander technique, Guided imagery, Hypnosis, Meditation, Rolfing/structural integration, Tai chi, Therapeutic touch, Yoga, Curanderismo, Native American medicine, Siddha medicine, Tibetan medicine or Anthroposophic medicine.

Treatment durations differed based on intervention type; for example, *Terminalia chebula* was administered for 5 days and osteopathy was studied in a six month period. Intervention durations were not prearranged in some studies such as Filho et al. (homeopathy) [49], Alcantara et al. (chiropractic) [41] and Iwai (Traditional Japanese Medicine) [30], instead being determined depending on patient conditions.

## Effectiveness of interventions

Most interventions had positive effects on childhood constipation, with the majority being statistically significant. An except was the Chmielewska research on the efficacy of glucomannan and its follow up study by Horvath et al. Likewise, Elbasan et al. could not demonstrate a positive effect of foot reflexology in children's constipation. A previous study by Canbulat Sahiner had also failed to demonstrate an effect for foot massage in such patients.

## Adverse effects

Reported adverse effect (AE) of interventions are listed in Table 2. Thirteen studies did not represent any information about AEs. In four studies no AE was observed, while no significant AEs were reported in yet three other research. Other studies reported gastrointestinal AEs, such as vomiting, diarrhea, abdominal pain and distention.

### Risk of bias of included studies

The quality assessment of included studies are listed in Tables 3 and 4.

## Discussion

Constipation is a common health problem in the pediatric population [54]. In this age group, constipation is a family issue that has a negative impact on children's physical, social, emotional, and school functions. Moreover, this condition has a significant impact on the use and cost of medical services [8].

Due to the various underlying causes of constipation in pediatrics, more treatment options are available compared to defaecatory dysfunction. This review focuses on the evidence for treatment options of this type of constipation based on CAM.

Insofar as we searched, our study is the first systematic review on the efficacy of various CAM interventions on pediatric constipation. A comprehensive search across multiple databases with no time limit ensured maximum results for the current study. A systematic review of herbal medicine efficacy in GI disorders (2017) [55] discovered one eligible study for herbal medicine in childhood constipation [25], whereas our study included ten studies in this field (See Table 1). In addition, we tried to include most CAM methods, even less recognized ones.

**Table 2** Adverse effects of interventions

| | First author (year) | Adverse effects |
|---|---|---|
| Herbal medicine | Day [20] (1995) | ND |
| | Loening-Baucke [21] (2004) | None |
| | Castillejo [22] (2006) | No significant adverse effect |
| | Ustunda [23] (2010) | Abdominal pain or distension, emesis, no significant difference between groups |
| | Chmielewska [24] (2011) | Similar in both groups (gastroenteritis possibly not related, vomiting probably related to medication) |
| | Quitadamo [25] (2012) | No significant adverse effect except for transient diarrhea, relieved by dose reduction |
| | Horvath [26] (2013) | ND |
| | Staiano [27] (1999) | None |
| | Perkin [28] (1977( | The number and frequency of side-effects (diarrhea, colic, distension) in senna treatment week were very much higher ($P < 0.001$) than in the lactulose week |
| | Closa-Monasterolo [29] (2017) | No increase in distension or flatulence |
| Traditional medicine | Iwai [30] (2007) | ND |
| | Mozaffarpur [31] (2012) | Diarrhea decreased by dose reduction (12 patients), sputum like stool (one patient) |
| | Nimrouzi [32] (2015) | Flatulence and Abdominal Pain<br>No significant difference between groups |
| | Esmaeilidooki [33] (2016) | CFE: Diarrhea (25%) and abdominal pain<br>(3.8%) ameliorated<br>by decreasing drug dose<br>PEG: (26.3%) diarrhea, (8.7%) abdominal pain relieved by dose adjustment, except for 1 patient. |
| | Shahamat [34] (2016) | ND |
| | Tajik [35] (2018) | No side effects |
| | Dehghani [36] (2019) | No significant side-effects, except for abdominal pain in seven patients in the PEG group and four in black strap molasses group in the first week of treatment, which disappeared with continuation of the treatment |
| | Mali [37] (2016) | ND |
| | Cai [38] (2018) | Loose stools, diarrhea and vomiting but no significant differences between groups |
| Manipulations | Broide [39] (2001) | ND |
| | Gordon [40] (2007) | None |
| | Alcantara [41] (2008) | ND |
| | Tarsuslu [42] (2009) | ND |
| | Silva [43] (2013) | None |
| | Bromley [44] (2014) | ND |
| | Orhan [45] (2016) | No serious side effects |
| | Elbasan [46] (2018) | ND |
| | Canbulat Sahiner [47] (2017) | ND |

**Table 2** (continued)

| | First author (year) | Adverse effects |
|---|---|---|
| | Zollars [48] (2018) | ND |
| Others | Filho [49] (2005) | ND |

*ND* Not Declared

Most CAM methods have their own rationales [56] those can influenced relevant researches. For example, blinding in some CAM interventions is a limitation. Designing a placebo for acupuncture, manual therapies and herbal remedies with their special smell, taste and color is a complex process with certain difficulties. However, it can partly be compensated by blinding evaluators [57], an issue that has been considered in some included studies.

Since diagnosis and treatment in CAM is usually complex and nonlinear [56], durations of interventions were determined individually in some studies. Nowadays, this is not an unusual approach as "Individualized Medicine" has emerged in medical literatures. Indeed, some attempts are being made to provide molecular biology evidences for individualized diagnostic and interventional approaches of many CAM modalities [58–61].

Diversity of treatment and follow up duration is another point. Perhaps shorter treatment duration is a variable that can result in better patients' compliance, although it does not guarantee more persistent outcomes necessarily.

The distinct circumstances of CAM modalities have motivated some methodologists to employ special methods [56] and checklists [62] to assess CAM studies, although most researchers still prefer common methods [63].

Some studies selected individuals with disabilities such as CP, or mentally disabled patients that can affect the outcomes. Nevertheless, we did not exclude such papers because little surveys were found in some types of interventions. Reasons may contain the less popularity of theme, small area in which they practiced, being hard to be examined in a standard trial or lack of efficient connections to scientific communities. Meanwhile, the number of pediatric surveys are generally less than studies conducted on adults. It can be interpreted on the basis of children studies nature that make their studies more difficult regarding medical ethics considerations.

Lack of control groups was a pitfall in some included studies that lowers the quality of such researches. Although many CAM interventions seem safe, monitoring and reporting adverse effects is imperative. This fact, which is a conclusion Wu TX et al. has declared about Chinese herbal medicine researches [64], was ignored in several included studies.

One of the main probable mechanisms of action for herbal drugs in constipation is the mechanism of fibers. Low-fiber intake has been associated with constipation in children [65]. Dietary fibers like glucomannan may influence defecation by several possible mechanisms: 1) the increased colonic contents may accelerate colonic transit and reduce colonic absorption of fluid; 2) fermentation of fiber releases gases, which may be trapped in colonic contents, contributing to their bulk; 3) the fiber may slow down absorption in the small intestine.

The results of the study by Closa-Monasterolo, reinforces the possible beneficial effects of the use of inulin-type fructans as fully fermentable dietary fibers from chicory roots to counteract constipation in young children and return bowel habits to a normal state [29].

Polysaccharides of molasses can serve as dietary fibers and bulking agents in the bowels. The naturally high potassium content of molasses syrup make this product an efficient treatment option for pediatric functional constipation [36].

Other mechanisms can also be considered for herbal remedies. Xiao'er Biantong which is a Chinese traditional remedy, consists of seven herbal medicine; each can take a role in ameliorating constipation via the following mechanisms: 1) acetyl choline and serotonin, which regulate GI motility, 2) magnolol, which can adjust brain function, 3) anthraquinones, which improve colon motor function, 4) reactive Aloeemodin, the drug metabolite by colonic flora that reinforces peristalsis and reduce fluid absorption via cholinergic receptors, 5) direct effect on specific on distal colon longitudinal muscles [38, 66–68].

Purgative mechanism of action of *D. sophia* has not been elucidated yet. Water absorbing mucilage may soften the stool. Allyl disulfide (sulfur glycoside such as descurainoside) in *D. sophia* seed may results in smooth muscles relaxation and assist to defecation [69]. Nor-lignans, secondary metabolites of the plant such as descuraic acid, can be effective in ameliorating constipation.

It seems that DKT display its laxative properties by contractile effect on small intestine [70].

Anthraquinone derivatives are the most probable responsible agents for cathartic and laxative effects of *Cassia fistula* fruits pulp [31, 71]. Anthraquinone glycone and anthraquinone glycosides are two forms of anthraquinones which have laxative properties. The degree of laxative potency is dependent on the content of anthraquinone [72].

Although more studies are needed to understand the exact mechanism of action of manual therapies, some mechanisms can be assumed. The effects of reflexology on constipation in

**Table 3** Quality assessment of included clinical trials

| | First author (year) | Randomization | | | Blinding | | | An account of all patients fate of all patients known, if not reason is stated | Score |
|---|---|---|---|---|---|---|---|---|---|
| | | Mentioned | Appropriate | Inappropriate | Mentioned | Appropriate | Inappropriate | | |
| Herbal medicine | Day [20] (1995) | 0 | | | 0 | | | 1 | 1 |
| | Loening-Baucke [21] (2004) | 1 | 1 | | 1 | 1 | | 1 | 5 |
| | Castillejo [22] (2006) | 1 | 1 | | 1 | 1 | | 1 | 5 |
| | Ustundag [23] (2010) | 1 | 1 | | 0 | | | 1 | 3 |
| | Chmielewska [24] (2011) | 1 | 1 | | 1 | 1 | | 1 | 5 |
| | Quitadamo [25] (2012) | 1 | 1 | | 0 | | | 1 | 3 |
| | Horvath [26] (2013) | 1 | 1 | | 1 | 1 | | 1 | 5 |
| | Staiano [27] (1999) | 1 | 0 | | 1 | 0 | | 1 | 3 |
| | PerKin [28] (1977( | 1 | 1 | | 0 | | | 1 | 3 |
| | Closa-Monasterolo [29] (2017) | 1 | 1 | | 1 | 1 | | 1 | 5 |
| Traditional medicine | Iwai [30] (2007) | 0 | | | 0 | | | 1 | 1 |
| | Mozaffarpur [31] (2012) | 1 | 1 | | 0 | | | 1 | 3 |
| | Nimrouzi [32] (2015) | 1 | 1 | | 0 | | | 1 | 3 |
| | Esmaeilidooki [33] (2016) | 1 | 1 | | 0 | | | 1 | 3 |
| | Shahamat [34] (2016) | 1 | 1 | | 0 | | | 1 | 3 |
| | Tajik [35] (2018) | 1 | 1 | | 0 | | | 1 | 3 |
| | Dehghani [36] (2019) | 1 | 1 | | 1 | 1 | | 1 | 5 |
| | Mali [37] (2016) | 0 | | | 0 | | | 1 | 1 |
| | Cai [38] (2018) | 1 | 1 | | 1 | 1 | | 1 | 5 |
| Manipulations | Broide [39] (2001) | 0 | | | 0 | | | 1 | 1 |
| | Gordon [40] (2007) | 1 | 1 | | 1 | 1 | | 1 | 5 |
| | Tarsuslu [42] (2009) | 0 | | | 0 | | | 0 | 0 |
| | Silva [43] (2013) | 1 | 1 | | 0 | | | 1 | 3 |
| | Bromley [44] (2014) | 0 | | | 0 | | | 1 | 1 |
| | Orhan [45] (2016) | 1 | 1 | | 0 | | | 1 | 3 |
| | Elbasan [46] (2018) | 1 | 1 | | 0 | | | 1 | 3 |
| | Canbulat Sahiner [47] (2017) | 1 | 0 | | 0 | | | 1 | 2 |

**Table 4** Quality assessment of included case series

| First author (year) | Risk of bias |
|---|---|
| Filho [49] (2005) | Moderate risk of bias |
| Alcantara [41] (2008) | Moderate risk of bias |
| Zollars [48] (2018) | Moderate risk of bias |

children with CP is exerted via the autonomous nervous system, specifically by increasing the activity of parasympathetic nervous system. A number of studies have reported stimulation of the autonomic nervous system by reflexology [46]. Likewise, visceral and neural manipulation affect the autonomic nervous system, often at the cranium, throughout the vagus nerves and the sacral plexus [48].

Our study encountered several limitations such as language limitation, as we included only English or Persian papers. We searched for every CAM therapy very carefully, but as CAM therapies are multifarious, we may have missed some types of CAM. Only published documents were included. Whereas CAM studies are more difficult to publish, there may be unpublished researches that are not included in our study. Another limitation that made some articles difficult to study and extract data was that in most CAM modalities an exclusive terminology is used, so acquaintance with the terminology is necessary to study these articles [37]. Unfortunately, as the number of studies in each method was limited, we could not perform any meta-analysis.

According to our systematic review, most studies reported significant effects for CAM interventions on children constipation without significant adverse effects; but to accept such conclusion, more studies with better qualities are required.

## Conclusion

There are not enough studies on the efficacy and safety of different types of complementary and alternative medicine methods in childhood constipation to conduct a meta-analysis, so conducting further high-quality research in each field is suggested. Available studies showed that CAM methods are usually effective and safe in childhood constipation. Designing studies to elucidate the mechanisms of CAM interventions in ameliorating constipation in children is also recommended. With higher levels of evidence, CAM therapies can be integrated into common therapies for childhood constipation.

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**Author contributions** MK made the main themes of the study. MSP searched databases and selected articles. MSP, MSM and SB assessed papers for eligibility, read full texts, filled a form for each one and assessed their quality. MSP created the table of results and wrote review draft. MK and PK reviewed the draft critically. MK was the guarantor of the study.

## Compliance with ethical standards

**Conflict of interest** None

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