Wangshi Baochi Pill for functional dyspepsia syndrome in infants and toddlers: a multicenter randomized placebo-controlled trial

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Background: Gastrointestinal discomfort in infants and toddlers is common, yet many cases may not meet the Rome IV diagnostic criteria, posing a challenge to clinical management. To address this gap, Chinese experts have proposed the novel diagnostic entity "functional dyspepsia syndrome in infants and toddlers" (FDSIT). Therapeutic options for functional gastrointestinal disorders in infants and toddlers remain considerably limited, particularly with regard to conventional Western pharmacotherapies. Wangshi Baochi Pill (WBP), a traditional Chinese medicine with a long history of pediatric use, has shown efficacy in older children (≥4 years) with functional dyspepsia. However, its efficacy and safety for FDSIT remain unclear. This study aimed to assess the efficacy and safety of WBP in infants and toddlers diagnosed with FDSIT according to the Chinese expert consensus.

Methods: This multicenter, randomized, double-blind, placebo-controlled trial was conducted across 15 hospitals in China. Eligible participants aged 1–36 months were randomly assigned (1:1, block size 4) to receive WBP (2 mg/kg twice daily) or a matching placebo for 7 days, with follow-up through day 14. The primary endpoint was the combined symptom effectiveness rate (CSER) at day 7, defined as the proportion of participants achieving a ≥50% reduction in total symptom score across five prespecified symptom domains,

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each graded on a 4-point scale. Secondary endpoints included CSER at days 3 and 14, individual symptom remission rates, growth parameters, and adverse events (AEs), which were systematically monitored via diary cards and clinical assessments.

Results: There were 240 infants and toddlers randomized; 229 were included in the full analytical set (WBP, n=113; placebo, n=116). Baseline characteristics were well balanced. At day 7, CSER was significantly higher in the WBP group than in the placebo group [69.03% *vs.* 33.62%; absolute difference 35.41%, 95% confidence interval (CI): 23.30% to 47.51%; χ^2=28.72, P<0.001]. Significant improvements with WBP were also observed at day 14 (82.30% *vs.* 43.97%; absolute difference 38.33%, 95% CI: 26.89% to 49.79%; χ^2=36.04, P<0.001). Symptom remission rates for decreased appetite, belching/abdominal distension/increased flatus, and abnormal defecation were significantly higher in the WBP group at both time points. AEs occurred in 19 (16.81%) WBP-treated participants and 17 (14.53%) placebo recipients (P=0.63). One mild episode of diarrhea (0.88%) in the WBP group was deemed a treatment-related adverse drug reaction. No serious AEs were reported.

Conclusions: In this trial, WBP demonstrated notable efficacy and a favorable short-term safety profile for the treatment of FDSIT. These findings suggest that WBP may represent a potential therapeutic option, although further confirmatory studies are warranted.

Trial Registration: Chinese Clinical Trial Registry (ChiCTR), ChiCTR2300072543. Registered on 16 June 2023.

Keywords: Functional dyspepsia syndrome (FD syndrome); infants and toddlers; Wangshi Baochi Pill (WBP); randomized controlled trial (RCT)

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Introduction

Gastrointestinal discomfort in infants and toddlers accounts for a substantial proportion of pediatric gastroenterology clinic visits (1). However, the duration and/or frequency of symptoms in many infants and toddlers do not meet the diagnostic thresholds of Rome IV criteria for functional gastrointestinal disorders, posing challenges to diagnosis and management (2,3). To address this gap, Chinese experts in pediatric gastroenterology have formulated the "Consensus on Diagnosis of Functional Dyspepsia Syndrome in Infants and Toddlers (FDSIT)", introducing the novel diagnostic entity of FDSIT for this age group (4). According to the consensus, FDSIT is defined as a common clinical condition characterized by recurrent symptoms including decreased appetite, belching/abdominal distension/increased flatus, nausea or vomiting, recurrent crying or abdominal pain, and abnormal defecation (increased frequency or volume of stools, loose or unformed stools, increased milk curds or undigested food residues in feces compared with usual, acidic or foul-smelling stools, hard stools, or bowel frequency >2 times per week without defecation difficulty), after appropriate medical evaluation to exclude organic diseases (4).

Although FDSIT is a functional disorder, it adversely affects the quality of life of children and imposes psychological and economic burdens on their families (5,6). Current management options for functional gastrointestinal disorders in this age group

Highlight box

Key findings

- Wangshi Baochi Pill (WBP) significantly improved overall symptoms in children with functional dyspepsia syndrome in infants and toddlers (FDSIT) at day 7.
- Efficacy was sustained through day 14 with no serious adverse events reported.
- Notable improvements were seen in decreased appetite, belching/

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distension/increased flatus, and abnormal defecation.

- WBP showed a favorable short-term safety profile in this vulnerable population.
- This randomized controlled trial provides preliminary evidence for WBP as a potential therapeutic option.

What is known and what is new?

- Management of FDSIT relies on reassurance and dietary advice; pharmacological options are limited. WBP has shown efficacy in older children (≥4 years) with functional dyspepsia.
- This first multicenter placebo-controlled trial demonstrates that a 7-day WBP regimen significantly improves key FDSIT symptoms—particularly decreased appetite, belching/distension/increased flatus, and abnormal defecation—with sustained benefit through day 14 and a favorable safety profile, suggesting that WBP may represent a potential therapeutic option for this pediatric population.

What is the implication, and what should change now?

- WBP can be considered a short-term therapeutic option for infants/toddlers with FDSIT, especially those with decreased appetite, belching/distension/increased flatus, or abnormal defecation, when conventional measures are insufficient.
- However, given the 7-day treatment window and lack of long-term safety data, clinicians should reserve use for symptomatic relief and monitor for mild diarrhea. Larger confirmatory trials and longer-term outcome studies are needed before routine adoption.

remain limited, focusing primarily on caregiver reassurance, nutritional guidance, and dietary modifications (7-9). Medications such as proton pump inhibitors or gastrointestinal motility agents are ineffective for infant regurgitation and may even increase the risk of infections (10). Although probiotics are widely used in clinical practice, current guidelines provide no specific probiotic recommendations for children with functional gastrointestinal disorders (11,12). Traditional Chinese Medicine (TCM) may offer a potential alternative. Adult studies have demonstrated that TCM is effective in treating functional gastrointestinal disorders (13). According to TCM theory, functional dyspepsia (FD) primarily arises from dysfunction of the spleen (Pi), stomach (Wei), and liver (Gan), with impaired transportation and transformation function of the spleen (Pi Yun Hua) and dispersing and descending function of the liver (Gan Shu Xie). TCM treatment employs holistic principles and syndrome differentiation to comprehensively regulate organ function, thereby restoring "Yin-Yang harmony" (Yin Yang Ping Heng) (14,15). Moreover, FDSIT presents with complex and variable symptoms that may overlap, requiring individualized and comprehensive treatment —this aligns well with the TCM principles of syndrome differentiation and holistic concept.

Wangshi Baochi Pill (WBP) is a TCM micro-pill formulation with a history of approximately 186 years of clinical use. It possesses well-defined pediatric indications and clear dosing instructions. Its main functions are removing stagnation, strengthening the spleen, and eliminating phlegm. It is primarily indicated for infantile milk stagnation (Ru Shi) and malnutrition accumulation (Gan Ji), phlegm-induced convulsion (Tan Jing), wheezing and productive cough with rales, decreased feeding or food intake, vomiting, diarrhea, and fever, constipation, seasonal common colds, spleen-stomach weakness (Pi Wei Xu Ruo) with poor physical development in gastrointestinal disorders in children and adults. Clinical studies have demonstrated its efficacy in functional gastrointestinal disorders in adults and children ≥4 years of age, including gastroesophageal reflux disease (GERD), chronic gastritis, FD, irritable bowel syndrome (IBS), and constipation (16). A 28-day repeated-dose toxicity study in juvenile rats conducted at Peking University showed no adverse effects on clinical signs, body weight, organ coefficients, biochemistry, or histopathology at doses up to 1,500 mg/kg/day, supporting the safety of WBP in clinical practice (17). However, its efficacy and safety in infants and toddlers with FDSIT have not been established. Therefore, this study aimed to evaluate the efficacy and safety of WBP in this population. We present this article in accordance with the CONSORT reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-2026-0479/rc).

Methods

Study design and participants

This multicenter, randomized, double-blind, placebo-controlled trial was conducted at the pediatrics or pediatric gastroenterology departments of 15 hospitals across China, with 16 patients enrolled at each site. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. This study was approved by the Ethics Committee of the leading hospital, Guangzhou Women and Children's Medical Center, Guangzhou Medical University (approval No. YW-202111). All participating hospitals were informed of and agreed to this study. Written informed

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consent was obtained from the legal guardians of all participants prior to enrollment. This trial was registered at chictr.org.cn (ChiCTR2300072543).

At each site, investigators screened consecutive outpatients presenting with gastrointestinal complaints during the enrollment period (November 22, 2021 – November 23, 2022). Eligible children were identified through initial clinical assessment; those meeting the diagnostic criteria for FDSIT (4) and no exclusion criteria were invited to participate. Participants were aged 1 to 36 months and had not received any medications affecting gastrointestinal function (e.g., antacids, acid-suppressing agents, or prokinetics) within the preceding week.

Major exclusion criteria included: (I) presence of organic gastrointestinal disorders, including peptic ulcer disease, malignancy, inflammatory bowel disease, pancreatitis, or intestinal tuberculosis; (II) severe cardiovascular, cerebrovascular, hepatic, renal, hematologic, connective tissue, or endocrine disorders; or psychiatric illness; (III) severe malnutrition; (IV) concomitant use of antacids, acid-suppressing agents, prokinetics, or other medications that may affect gastrointestinal function; (V) known hypersensitivity to WBP or any of its components; (VI) participation in another intervention study within the 12 weeks prior to screening; or (VII) any other condition deemed by the investigators to render the child ineligible.

Randomization and masking

A total of 240 participants were enrolled across 15 study centers, with a planned enrollment of 16 participants per center. This trial employed a double-blind design with two-level blinding. At the first level, treatments were coded as Group A and Group B; at the second level, the actual treatment assignments for Group A and Group B were specified. The randomization sequence was generated using the PROC PLAN procedure in SAS version 9.4 (fixed seed number =20,210,918) with a block size of 4. A total of 60 blocks were generated, with a 1:1 allocation ratio between WBP and placebo, yielding a random treatment assignment for all 240 participants. A treatment allocation list corresponding to sequential numbers 001 through 240 was produced, generating the Randomization Code List for the Trial (first-level blinding code), the Treatment Group Allocation (second-level blinding code), and other related documents. All blinding codes were sealed and stored securely.

Consecutive blocks of sequential numbers were assigned to each center according to the order of site initiation, and investigators allocated these numbers sequentially based on participant enrollment order.

Blinding preparation, including the preparation of emergency unblinding envelopes, was performed by an independent statistician not involved in the trial. The entire drug coding process was documented by the blinded statistician in a Blinding Record, which was archived. Medication kits were prepared according to participant number and treatment group, with the kit number matching the participant number. Emergency unblinding envelopes, labeled with the participant number and containing the randomization code and group assignment, were prepared and distributed to each participating center. The envelopes were clearly marked with the participant number on the outside and were strictly prohibited from being opened except in an emergency.

To maintain blinding, a matching placebo identical to WBP in appearance, texture, color, odor, and taste was used; it contained 10% active ingredient (18-20). Both WBP

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and placebo were manufactured by Jinghua Pharmaceutical Co., Ltd. (Nantong, China) (National Medical Product Approval Number: Z32020645).

Study procedures

Following randomization, all participants underwent baseline assessments, including demographic and clinical characteristics, growth parameters, and symptom severity evaluation using the Infant Functional Dyspepsia Syndrome Symptom Scale (Table S1). This scale, developed based on the Chinese expert consensus (4), comprises five symptom domains, each graded on a 4-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe), with individual and total scores recorded for each participant.

Participants received either WBP or placebo orally at 2 mg/kg twice daily for 7 days, with follow-up through day 14. Study visits occurred at three time points: telephone follow-up (day 3±1), clinic visit (day 7±1), and final evaluation (day 14±2). At each visit, symptom scores were reassessed using the same scale, growth parameters (length, weight, head circumference) were measured during clinic visits only, and adverse events (AEs) and medication adherence were documented. From baseline, caregivers were provided with diary cards for daily recording of symptoms and medication intake until study completion. Medication adherence was calculated as (actual dose taken/prescribed dose) ×100%, with compliance defined as 80–120% of the prescribed dose; adherence data were derived from diary card records and verified at each visit.

Outcomes

The primary endpoint was the Combined Symptom Effectiveness Rate (CSER) at day 7, calculated using the Infant Functional Dyspepsia Syndrome Symptom Scale, which was developed based on the Chinese expert consensus. CSER was defined as the proportion of participants achieving a "markedly effective" or "effective" response: markedly effective was defined as a ≥75% reduction in total symptom score; effective as a 50% to <75% reduction; and ineffective as a <50% reduction or symptom worsening.

The secondary endpoints included: (I) CSER at days 3 and 14; (II) remission rates for individual symptoms at days 3 and 7, where "resolved" was defined as a symptom score of 0, "improved" as a 1- to 2-grade reduction without complete resolution, and "ineffective" as no improvement or worsening; (III) growth parameters (length, weight, and head circumference) measured at days 7 and 14; and (IV) recurrence rate within 7 days post-treatment, defined as the return of symptoms (total score >0) at day 14 following complete resolution (score =0) at day 7.

Safety assessment

AEs were collected at each visit via active caregiver inquiry and daily diary cards. AEs were coded using Medical Dictionary for Regulatory Activities (MedDRA), graded according to Common Terminology Criteria for Adverse Events (CTCAE), and assessed for causality by the investigators using Council for International Organizations of Medical Sciences (CIOMS) criteria. Serious adverse events (SAEs) were defined per International Council for Harmonisation E2A (ICH E2A) guidelines and reported within 24 hours. Safety data were reviewed periodically by designated personnel at each

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center. Safety endpoints included the incidence rates of AEs and adverse drug reactions (ADRs).

Sample size

This study employed a superiority design. Assuming a 75% response rate in the WBP group and 35% in the placebo group after 7 days of treatment, with a superiority margin of 20%, a one-sided alpha of 0.025, and a power of 80%, 93 participants per group were required under a 1:1 allocation. Accounting for a 20% dropout rate, 120 participants were enrolled per group, totaling 240 participants.

Statistical analysis

Continuous variables were summarized as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Between-group comparisons were performed using independent-samples t-tests or Wilcoxon rank-sum tests for continuous variables, and chi-square or Fisher's exact tests for categorical variables, as appropriate. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). All tests were two-sided, and a $P<0.05$ was considered statistically significant.

The Full Analysis Set (FAS), defined as all randomized participants who received at least one dose of the study drug and had at least one post-baseline efficacy assessment, served as the primary analysis set for efficacy. The Per-Protocol Set (PPS), comprising FAS participants without major protocol deviations, was used for supportive sensitivity analyses. The Safety Analysis Set (SS), defined as all randomized participants who received at least one dose of the study medication and had at least one post-dose safety assessment, was used for safety evaluations.

Results

Enrollment

Between November 2021 and November 2022, of 243 patients assessed for eligibility, 240 were enrolled and randomly assigned to the WBP group (n=120) or the placebo group (n=120). A detailed center-specific case distribution is provided in Table S2. Two hundred and twenty-four participants (111 in the WBP group and 113 in the placebo group) completed the trial per protocol, while 16 participants discontinued (9 in the WBP group and 7 in the placebo group) primarily owing to parental/guardian consent withdrawal or AEs (*Figure 1*). FAS comprised 229 participants (113 in the WBP group and 116 in the placebo group), excluding 7 participants in the WBP group and 4 in the placebo group who were withdrawn after randomization but before receiving any study treatment. PPS included 203 participants (99 in the WBP group and 104 in the placebo group), with 12 participants in the WBP group and 9 in the placebo group excluded due to protocol violations. SS included 230 participants.

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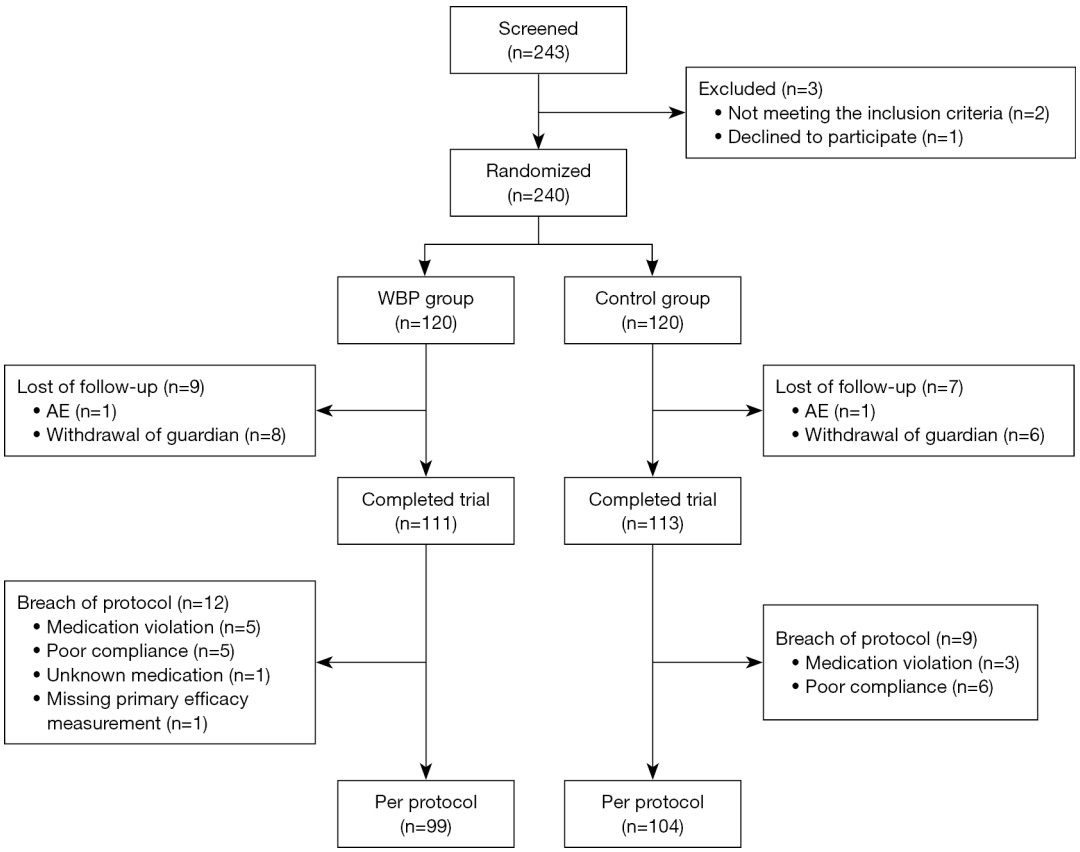


Figure 1 Flow diagram. WBP, Wangshi Baochi Pill. AE, adverse event.

Baseline characteristics of participants

Baseline characteristics are shown in *Table 1*. In the FAS, the WBP group comprised 113 participants [54 male (47.79%) and 59 female (52.21%)], whereas the placebo group comprised 116 participants [63 male (54.31%) and 53 female (45.69%)]. The mean age was 18.83±9.91 months in the WBP group and 20.08±9.81 months in the placebo group. No significant differences were observed between the two groups with respect to sex distribution, age, body length, weight, head circumference, or ethnicity. The median symptom duration was comparable between the two groups (32.00 days in the WBP group *vs.* 30.00 days in the placebo group), as was the total symptom score (4.02±1.34 *vs.* 3.98±1.84) and the distribution of symptom severity (mild, moderate, severe).

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Table 1 Baseline characteristics of participants

Characteristics	WBP group (n=113)	Placebo group (n=116)	P
Age (months)	18.83±9.91	20.08±9.81	0.32
Sex			
Male	54 (47.79)	63 (54.31)	0.32
Female	59 (52.21)	53 (45.69)	
Body length (cm)	80.19±10.77	80.70±10.67	0.64
Body weight (kg)	10.49±2.62	10.62±2.62	0.54
Head circumference (cm)	45.81±2.97	45.95±3.34	0.53
Race			
The Han nationality	98 (86.73)	106 (91.38)	0.25
Other nationality	15 (13.27)	10 (8.62)	
Course (days)	32.00 (21.00, 90.00)	30.00 (20.00, 65.00)	0.48
Total score of functional dyspepsia symptoms (points)	4.02±1.34	3.98±1.84	0.23
Decreased appetite (points)			
0	27 (23.89)	34 (29.31)	0.84
1	54 (47.79)	46 (39.66)	
2	28 (24.78)	30 (25.86)	
3	4 (3.54)	6 (5.17)	
Increased belching/abdominal distension/increased flatulence (points)			
0	43 (38.05)	38 (32.76)	0.40
1	47 (41.59)	52 (44.83)	
2	21 (18.58)	21 (18.10)	
3	2 (1.77)	5 (4.31)	
Nausea or vomiting (points)			
0	89 (78.76)	87 (75.00)	0.47
1	19 (16.81)	22 (18.97)	
2	5 (4.42)	5 (4.31)	
3	0 (0.00)	2 (1.72)	
Recurrent crying or abdominal pain (points)			
0	69 (61.06)	69 (59.48)	>0.99
1	24 (21.24)	32 (27.59)	
2	14 (12.39)	7 (6.03)	
3	6 (5.31)	8 (6.90)	
Abnormal defecation (points)			
0	14 (12.39)	22 (18.97)	0.054
1	67 (59.29)	72 (62.07)	
2	25 (22.12)	17 (14.66)	
3	7 (6.19)	5 (4.31)	

Data are presented as n (%), mean ± standard deviation, or median (interquartile range). WBP, Wangshi Baochi Pill.

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Efficacy outcomes

Table 2 and *Figure 2* show the changes in total symptom scores over time. At baseline, mean scores were comparable between groups (4.02±1.34 *vs.* 3.98±1.84; Z=1.19, P=0.23). At day 3, both groups showed modest reductions in symptom severity (3.07±1.50 *vs.* 3.33±1.71), with no significant between-group difference (Z=–1.19, P=0.23). At day 7, however, the WBP group demonstrated a significantly greater reduction in symptom scores than the placebo group (1.85±1.10 *vs.* 2.65±1.67; Z=–3.82, P<0.001). This treatment effect was sustained through day 14, with WBP continuing to show greater improvement than placebo (1.41±1.27 *vs.* 2.31±1.71; Z=–4.59, P<0.001).

Table 2 Total symptom scores at different time points between two groups

Time points	WBP group (n=113)	Placebo group (n=116)	Statistic	P value
Baseline	4.02±1.34	3.98±1.84	Z=1.1875	0.23
Day 3	3.07±1.50	3.33±1.71	Z=–1.1887	0.23
Day 7	1.85±1.10	2.65±1.67	Z=–3.8183	<0.001
Day 14	1.41±1.27	2.31±1.71	Z=–4.5932	<0.001

Data are presented as mean ± standard deviation. WBP, Wangshi Baochi Pill.

In the FAS, the primary endpoint of CSER at day 7 was significantly higher in the WBP group (78/113, 69.03%) than in the placebo group [39/116, 33.62%; absolute difference 35.41%, 95% confidence interval (CI): 23.30% to 47.51%; χ^2=28.72, P<0.001], exceeding the prespecified superiority margin of 20%. The WBP group also showed significantly higher rates of both markedly effective (26/113, 23.01% *vs.* 10/116, 8.62%) and effective responses (52/113, 46.02% *vs.* 29/116, 25.00%), with a significant between-group difference in the ordinal efficacy distribution (Z=–5.32, P<0.001) (*Table 3* and *Figure 3*).

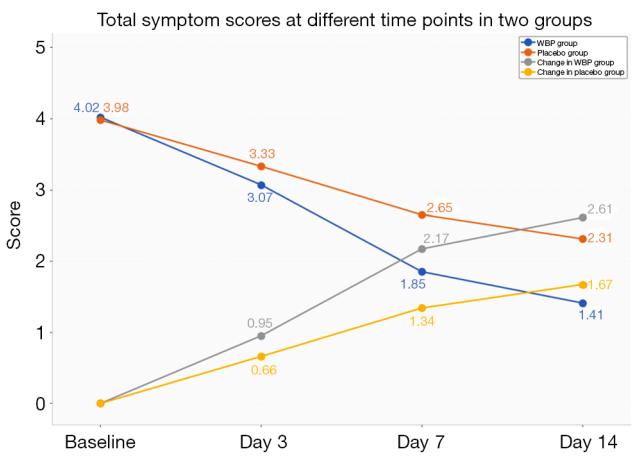


Figure 2 Total symptom scores at different time points in two groups. WBP, Wangshi Baochi Pill.

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Table 3 The CSER at different time points in two groups

Efficacy	Trial group (n=113)	Control group (n=116)	Statistic	P value
Day 3				
Efficacy composition			Z=−2.3407	0.01
Markedly effective	8 (7.08)	8 (6.90)		
Effective	19 (16.81)	5 (4.31)		
Ineffective	86 (76.11)	103 (88.79)		
CSER			χ^2=6.3909	0.01
Effective	27 (23.89)	13 (11.21)		
Ineffective	86 (76.11)	103 (88.79)		
Day 7				
Efficacy composition			Z=−5.3211	<0.001
Markedly effective	26 (23.01)	10 (8.62)		
Effective	52 (46.02)	29 (25.00)		
Ineffective	35 (30.97)	77 (66.38)		
CSER			χ^2=28.7156	<0.001
Effective	78 (69.03)	39 (33.62)		
Ineffective	35 (30.97)	77 (66.38)		
Day 14				
Efficacy composition			Z=−5.8794	<0.001
Markedly effective	54 (47.79)	24 (20.69)		
Effective	39 (34.51)	27 (23.28)		
Ineffective	20 (17.70)	65 (56.03)		
CSER			χ^2=36.0404	<0.001
Effective	93 (82.30)	51 (43.97)		
Ineffective	20 (17.70)	65 (56.03)		

Data are presented as n (%). CSER, combined symptom effectiveness rate.

At day 3, the CSER was higher in the WBP group than in the placebo group (27/113, 23.89% *vs.* 13/116, 11.21%; χ^2=6.39, P=0.01), driven by a significantly higher effective response rate (19/113, 16.81% *vs.* 5/116, 4.31%). The between-group difference in ordinal efficacy distribution was also significant (Z=−2.34, P=0.02). At day 14, the CSER remained significantly higher in the WBP group (93/113, 82.30% *vs.* 51/116, 43.97%; absolute difference 38.33%, 95% CI: 26.89% to 49.79%; χ^2=36.04, P<0.001), with significantly higher rates of both markedly effective (54/113, 47.78% *vs.* 24/116, 20.68%) and effective responses (39/113, 34.51% *vs.* 27/116, 23.28%); the ordinal efficacy difference was also significant (Z=−5.88, P<0.001) (*Table 3* and *Figure 3*).

At day 7 and day 14, WBP was associated with significantly higher remission rates than placebo for decreased appetite (55.81% *vs.* 32.93%; χ^2=8.90, P=0.003 and 70.93% *vs.* 37.80%; χ^2=18.59, P<0.001), belching/abdominal distension/increased flatus (50.00% *vs.* 26.92%; χ^2=8.35, P=0.004 and 62.86% *vs.* 34.62%; χ^2=11.79, P<0.001), and abnormal defecation (31.31% *vs.* 13.83%; χ^2=8.37, P=0.004 and 45.45% *vs.* 27.66%;

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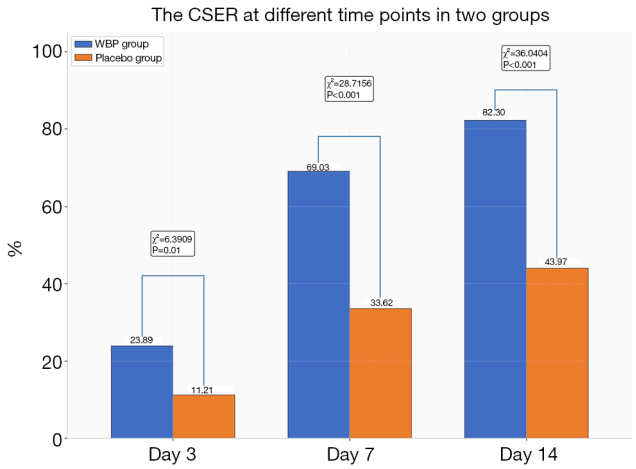


Figure 3 The CSER at different time points in two groups. CSER, combined symptom effectiveness rate; WBP, Wangshi Baochi Pill.

χ^2=6.57, P=0.01). No significant differences were observed between groups at day 3 for these symptoms (*Table 4*). For nausea/vomiting and recurrent crying/abdominal pain, no significant between-group differences were observed at any time point (*Table 4* and *Figure 4*).

Growth parameters, including weight, length, and head circumference, were assessed at baseline and on days 7 and 14. No clinically meaningful between-group differences were observed at any time point throughout the study period. The recurrence rate was not analyzed due to an insufficient number of participants achieving complete resolution of all dyspeptic symptoms at 1 week post-treatment (*Table 5*).

AEs

A total of 230 enrolled participants were included in the safety analysis set. During the trial period, AEs occurred in 36 participants (19 in the WBP group and 17 in the placebo group). The overall incidence of AEs was comparable between the WBP group (16.81%) and the placebo group (14.53%), with no statistically significant difference (χ^2=0.23, P=0.63). All AEs were graded as Grade 1 (mild) according to CTCAE criteria. One AE (diarrhea) in the WBP group was assessed as related to the study treatment, yielding an ADR incidence of 0.88%. No SAEs were reported (*Table 6*).

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Table 4 Efficacy and remission rates of individual symptoms at different time points

Symptom/outcome	Day 3				Day 7				Day 14			
	WBP	Placebo	χ^2	P	WBP	Placebo	χ^2	P	WBP	Placebo	χ^2	P
Decreased appetite			1.4571	0.22			8.8973	0.002			18.5926	<0.001
Complete remission	20 (23.26)	13 (15.85)			48 (55.81)	27 (32.93)			61 (70.93)	31 (37.80)		
Partial response	12 (13.95)	11 (13.41)			13 (15.12)	19 (23.17)			10 (11.63)	22 (26.83)		
Non-response	54 (62.79)	58 (70.73)			25 (29.07)	36 (43.90)			15 (17.44)	29 (35.37)		
Belching/abdominal distension/increased flatus			1.8552	0.17			8.3528	0.003			11.7893	<0.001
Complete remission	17 (24.29)	12 (15.38)			35 (50.00)	21 (26.92)			44 (62.86)	27 (34.62)		
Partial response	9 (12.86)	12 (15.38)			13 (18.57)	18 (23.08)			8 (11.43)	18 (23.08)		
Non-response	44 (62.86)	54 (69.23)			22 (31.43)	39 (50.00)			18 (25.71)	33 (42.31)		
Nausea/vomiting			0.0004	0.98			0.0314	0.85			0.3618	0.54
Complete remission	10 (41.67)	12 (41.38)			13 (54.17)	15 (51.72)			16 (66.67)	17 (58.62)		
Partial response	1 (4.17)	3 (10.34)			3 (12.50)	3 (10.34)			2 (8.33)	3 (10.34)		
Non-response	13 (54.17)	14 (48.28)			8 (33.33)	11 (37.93)			6 (25.00)	9 (31.03)		
Recurrent crying/abdominal pain			0.1775	0.67			1.2378	0.26			0.1105	0.73
Complete remission	11 (25.00)	10 (21.28)			20 (45.45)	16 (34.04)			24 (54.55)	24 (51.06)		
Partial response	9 (20.45)	8 (17.02)			13 (29.55)	9 (19.15)			7 (15.91)	8 (17.02)		
Non-response	24 (54.55)	29 (61.70)			11 (25.00)	22 (46.81)			13 (29.55)	15 (31.91)		
Abnormal defecation			1.5560	0.24			8.9612	0.002			6.9942	0.008
Complete remission	13 (15.12)	8 (9.30)			30 (34.88)	13 (15.12)			43 (50.00)	26 (30.23)		
Partial response	8 (9.30)	5 (5.81)			19 (22.09)	16 (18.60)			12 (13.95)	11 (12.79)		
Non-response	65 (75.58)	73 (84.88)			37 (43.02)	57 (66.28)			31 (36.05)	49 (56.98)		

Data are presented as n (%). WBP, Wangshi Baochi Pill.

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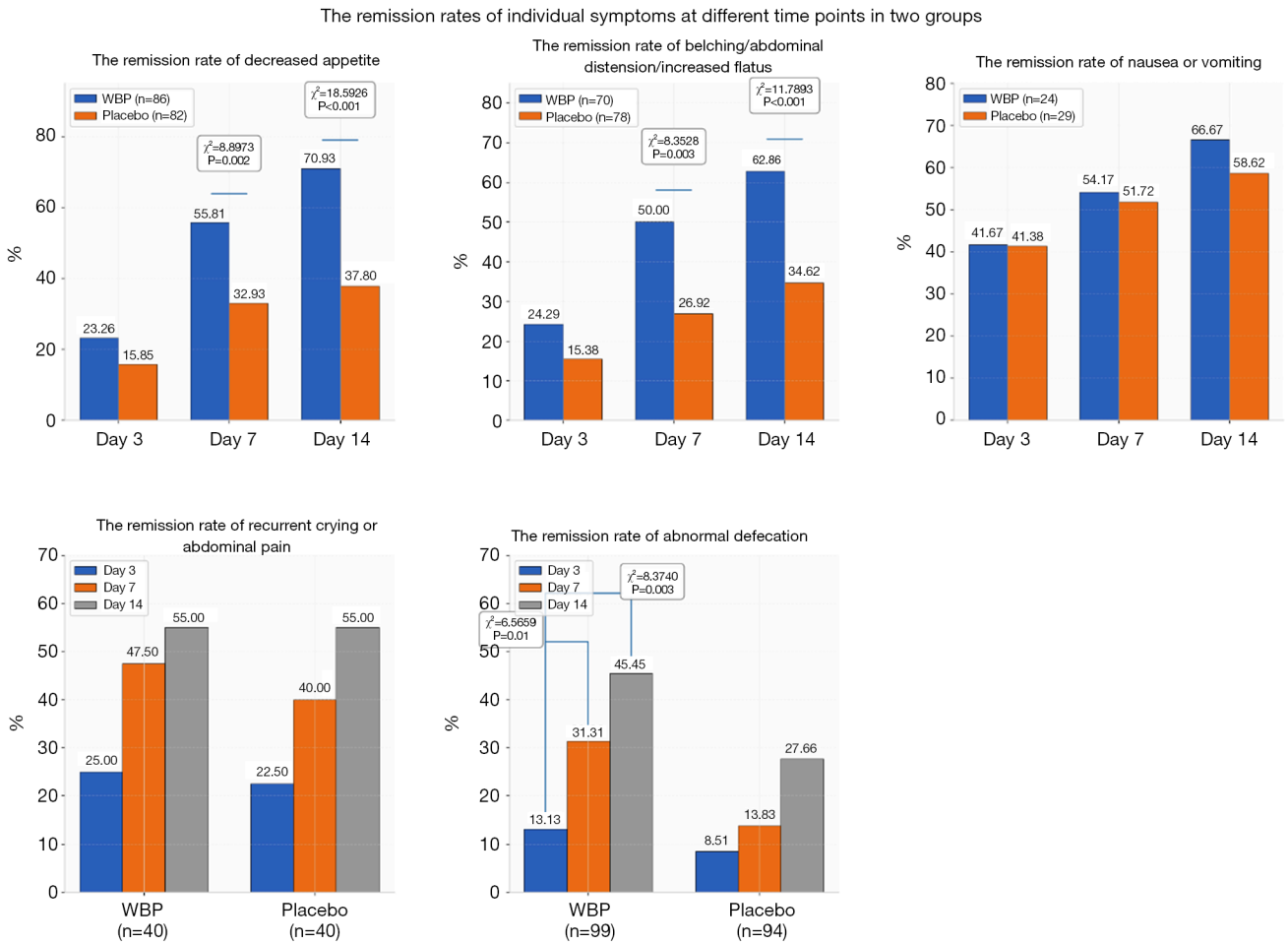


Figure 4 The remission rate of individual symptoms at different time points in two groups. WBP, Wangshi Baochi Pill.

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Table 5 The growth and development indicators of children at different time points

Growth and development indicators	WBP group (n=113)	Placebo group (n=116)	P
Baseline			
Weight (kg)	10.67±2.64	10.71±2.79	0.75
Length (cm)	80.66±10.93	80.94±11.07	0.86
Head circumference (cm)	45.94±2.93	45.85±3.54	0.87
Day 3			
Weight (kg)	10.66±2.64	10.71±2.78	0.75
Length (cm)	80.68±10.95	80.98±11.05	0.85
Head circumference (cm)	45.95±2.92	45.93±3.51	0.82
Day 7			
Weight (kg)	10.75±2.64	10.79±2.75	0.92
Length (cm)	80.84±10.80	80.99±10.99	0.92
Head circumference (cm)	46.05±2.82	46.00±3.46	0.86
Day14			
Weight (kg)	10.82±2.64	10.89±2.74	0.86
Length (cm)	80.99±10.78	81.16±10.92	0.92
Head circumference (cm)	46.04±2.80	46.02±3.45	0.82

Data are presented as mean ± standard deviation. WBP, Wangshi Baochi Pill.

Table 6 AEs by system organ class and preferred term

System organ class and preferred term	WBP group (n=113)	Placebo group (n=117)
Number of patients with AEs	19 (16.81)	17 (14.53)
Gastrointestinal disorders		
Diarrhea	5	5
Nausea/vomiting	3	0
Belching	0	1
Infections and infestations		
Fever	2	0
Respiratory or thoracic disorders		
Acute upper respiratory infection	7	6
Acute bronchitis	1	1
Acute tonsillitis	0	1
Skin and subcutaneous tissue disorders		
Dermatitis	1	3

Data are presented as n (%) or n. All AEs were mild (grade 1) or moderate (grade 2). One AE (diarrhea) in the WBP group was assessed as related to the study treatment. AEs, adverse events; WBP, Wangshi Baochi Pill.

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Discussion

This multicenter, randomized, double-blind, placebo-controlled trial is the first to evaluate the efficacy and safety of WBP in FDSIT. Of the 240 enrolled participants, 229 were included in the FAS (113 in the WBP group and 116 in the placebo group). Participants ranged in aged 1 to 35 months, with mean ages of 18.83±9.91 and 20.08±9.81 months in the WBP and placebo groups, respectively. Both groups had a male-to-female ratio of approximately 1:1, and the median symptom duration at baseline was 30 days and 32 days, respectively. The total symptom score was 4.02±1.34 in the WBP group and 3.98±1.84 in the placebo group. Baseline characteristics, including sex distribution, anthropometric measures, symptom duration, and total symptom scores, were well balanced between groups.

At day 7, the WBP group showed a significantly greater reduction in total symptom scores compared with the placebo group, with a correspondingly higher CSER. This improvement was sustained through day 14, with no evidence of symptom recurrence during the follow-up period. WBP also yielded significantly higher remission rates at day 7 for decreased appetite, belching/abdominal distension/increased flatus, and abnormal defecation. However, no significant differences were observed at day 3, suggesting that treatment effects may require more than one week to manifest. These findings are consistent with earlier studies in children aged ≥4 years with FD (21) and align with previous reports showing WBP efficacy in appetite, anorexia, abdominal distension and constipation (22-25).

In contrast to earlier studies that reported WBP benefits for abdominal pain (22,23), our trial did not detect significant improvements in recurrent crying/abdominal pain or nausea/vomiting. This discrepancy may reflect differences in the study population (infants *vs.* older children), symptom definitions, or the self-limiting nature of these symptoms in this age group. Due to the short intervention period (7 days), no clinically meaningful changes in growth parameters (body length, weight, head circumference) were observed. The recurrence rate was not analyzed due to insufficient cases of complete symptom resolution at 1 week post-treatment.

WBP is a traditional Chinese herbal preparation composed of multiple ingredients, including *Coptis chinensis*, *Rheum officinale*, *Fritillaria cirrhosa*, croton cream, prepared *Arisaema consanguineum*, and dried ginger. According to TCM theory, *Coptis chinensis* and *Rheum officinale* can clear heat, remove dampness, invigorate the spleen, and reduce fire; *Fritillaria cirrhosa*, croton cream, and prepared *Arisaema consanguineum* act to eliminate food accumulation; supplemented with dried ginger, it can warm the middle and harmonize the stomach. When used in combination, these herbs jointly exert the efficacy of clearing heat and dampness, invigorating the spleen and promoting digestion. Moreover, the prescription combines both cold and warm herbs, attacks accumulated food and resolves stagnation. It can regulate gastrointestinal functions, incorporate nourishment during elimination, invigorate the spleen and benefit the stomach, and play a role in promoting the transportation and transformation of essential substances.

Modern pharmacological studies have demonstrated that WBP promotes gastric pepsin activity, accelerates gastric emptying, modulates gastrointestinal smooth muscle tone, and protects the gastric mucosa (26-28). Animal studies have further shown that WBP modulates gut microbiota composition by increasing the abundance of short-chain fatty acid-producing bacteria (e.g., *Ruminiclostridium*-9 and *Eubacterium ventriosum*) while reducing inflammation-associated taxa such as *Jeotgalicoccus* and

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Bilophila (28). These findings are consistent with its clinically observed bidirectional effects on constipation and diarrhea. Network pharmacology analyses suggest that its main active components—curcumin, emodin, quercetin, and β-sitosterol—may act through multiple signaling pathways, including NF-κB and calcium signaling, to alleviate functional gastrointestinal symptoms (29). Collectively, these mechanistic insights support the potential of WBP in treating decreased appetite, constipation, belching, and abdominal distension in the context of FD syndrome.

Assessment of growth parameters revealed no clinically meaningful changes in length, weight, or head circumference throughout the 14-day study period in either treatment group. This finding is reassuring, given the importance of growth monitoring in pediatric patients with functional gastrointestinal disorders. The absence of adverse effects on growth parameters during this short-term follow-up supports the potential suitability of WBP for use in this age group.

Drug safety is a critical consideration in clinical research on TCM. All safety assessments, including AE coding, grading, and causality adjudication, were performed in accordance with international guidelines (MedDRA, CTCAE, and CIOMS criteria), ensuring the rigor and transparency of our safety reporting. In this study, one child in the WBP group experienced mild diarrhea after medication administration, which resolved spontaneously without intervention. No serious adverse reactions were reported. The mild diarrhea may be consistent with the rhubarb, a constituent of WBP with laxative properties. Although diarrhea may occur as a potential adverse effect of WBP, it is generally mild and can be alleviated by discontinuation of the drug. Collectively, these findings support favorable short-term safety profiles of WBP in the clinical management of FDSIT.

In this study, data from the placebo group demonstrated a reduction in total symptom scores from 3.98 to 2.31 over the two-week follow-up period, although the degree of improvement was less pronounced than that observed in the WBP group. The CSER in the placebo group was 43.97%, compared with 82.30% in the WBP group. At day 14, the remission rates for decreased appetite, belching/abdominal distension/increased flatus, and abnormal defecation in the placebo group were 37.8%, 34.62%, and 27.66%, respectively, suggesting that approximately one-third of infants and toddlers may experience symptom resolution without active treatment. In contrast, the remission rates for nausea or vomiting and recurrent crying or abdominal pain were 58.62% and 51.06%, respectively, with no significant differences compared with the WBP group. These findings suggest that over half of infants and toddlers with nausea, vomiting, recurrent crying, or abdominal pain may experience spontaneous symptom resolution without pharmacological intervention, achieving outcomes comparable to medication. This pattern aligns with epidemiological observations that infant regurgitation tends to improve with age, while infant colic typically occurs between 1 and 4 months of age and resolves spontaneously within 3 to 4 months (30,31). Collectively, these findings suggest that nausea/vomiting and recurrent crying/abdominal pain have a higher likelihood of spontaneous resolution; however, this inference requires confirmation through prospective longitudinal cohort studies.

Several limitations of this study should be acknowledged. First, all enrolled participants were recruited from patients attending pediatrics or pediatric gastroenterology departments, the study sample may not fully represent the general population of FDSIT, the exclusion of infants younger than 1 month and the potential

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selection bias toward enrollment of infants>6 months may limit the generalizability of the findings to the broader infant and toddler population. Second, the 7-day treatment duration, while sufficient to demonstrate short-term efficacy, precludes assessment of long-term safety and sustained therapeutic effects beyond the treatment period. The inability to analyze recurrence rates due to insufficient cases of complete symptom resolution at Week 1 represents a missed opportunity to evaluate durability of response. Third, the reliance on caregiver-reported symptom scales introduces potential subjectivity in outcome assessment, despite the use of validated instruments. Fourth, the study did not incorporate objective measures of gastric emptying or gastrointestinal motility, which could elucidate the mechanistic pathways underlying WBP efficacy.

The findings of this trial have implications for clinical practice. Current management strategies for FDSIT are largely limited to reassurance, dietary modifications, and nutritional interventions, with pharmacological options lacking robust evidence or regulatory approval for this age group. In this trial, WBP demonstrated notable efficacy and a favorable short-term safety profile, suggesting that it may represent a potential therapeutic option for symptomatic infants and toddlers, particularly those with predominant symptoms of decreased appetite, belching/abdominal distension, and abnormal defecation. However, given the methodological constraints of this study, further confirmatory studies are warranted to establish the clinical utility of WBP in this population. Future research should focus on: (I) long-term randomized controlled trials to evaluate sustained efficacy, recurrence rates, and long-term safety; (II) mechanistic studies utilizing objective gastrointestinal function assessments.

Conclusions

In this multicenter, randomized, double-blind, placebo-controlled trial, WBP demonstrated notable efficacy and a favorable short-term safety profile in the treatment of FDSIT. The treatment effects were most prominent for decreased appetite, belching/abdominal distension/increased flatus, and abnormal defecation. These findings suggest that WBP may represent a potential therapeutic option for FD syndrome in this pediatric population.

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Footnote

Reporting Checklist: The authors have completed the CONSORT reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-2026-0479/rc

Trial Protocol: Available at https://tp.amegroups.com/article/view/10.21037/tp-2026-0479/tp

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. This study was approved by the Ethics Committee of the leading hospital, Guangzhou Women and Children's Medical Center, Guangzhou Medical University (approval No. YW-202111). All

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participating hospitals were informed of and agreed to this study. All legal guardians of study participants were provided with verbal and written information about this study, and written informed consent was obtained prior to enrollment.

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References

1. Ferreira-Maia AP, Matijasevich A, Wang YP. Epidemiology of functional gastrointestinal disorders in infants and toddlers: A systematic review. World J Gastroenterol 2016;22:6547-58.
2. Drossman DA. Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV. Gastroenterology 2016. [Epub ahead of print]. doi: 10.1053/j.gastro.2016.02.032.
3. Howard CR, Lanphear N, Lanphear BP, et al. Parental responses to infant crying and colic: the effect on breastfeeding duration. Breastfeed Med 2006;1:146-55.
4. Subspecialty Group of Gastroenterology, China Association of Traditional Chinese Medicine Children's Health and Drug Research Professional Committee; Subspecialty Group of Gastroenterology, the Society of Pediatrics, Chinese Medical Association; Editorial Board, Chinese Journal of Pediatrics. Expert consensus on the diagnosis of functional dyspepsia syndrome in infant and toddler. Zhonghua Er Ke Za Zhi 2022;60:618-20. [Article in Chinese].
5. Morais MB. Signs and symptoms associated with digestive tract development. J Pediatr (Rio J) 2016;92:S46-56.
6. Vandenplas Y, Hauser B, Salvatore S. Functional Gastrointestinal Disorders in Infancy: Impact on the Health of the Infant and Family. Pediatr Gastroenterol Hepatol Nutr 2019;22:207-16.
7. Salvatore S, Abkari A, Cai W, et al. Review shows that parental reassurance and nutritional advice help to optimise the management of functional gastrointestinal disorders in infants. Acta Paediatr 2018;107:1512-20.
8. Gong ST. Improve the understanding of functional dyspepsia syndrome in infant and toddler. Zhonghua Er Ke Za Zhi 2022;60:615-7. [Article in Chinese].
9. The Subspecialty Group of Gastroenterology, Society of Pediatrics, Chinese Medical Association; Editorial Board of Chinese Journal of Pediatrics. Expert consensus on non-pharmacological interventions for infant functional dyspepsia syndrome (2024). Chinese Journal of Pediatrics 2024;62:514-9.
10. Blank ML, Parkin L. National Study of Off-label Proton Pump Inhibitor Use Among New Zealand Infants in the First Year of Life (2005-2012). J Pediatr Gastroenterol Nutr 2017;65:179-84.

11. Pärtty A, Rautava S, Kalliomäki M. Probiotics on Pediatric Functional Gastrointestinal Disorders. Nutrients 2018;10:1836.
12. Scarpato E, Quitadamo P, Roman E, et al. Functional Gastrointestinal Disorders in Children: A Survey on Clinical Approach in the Mediterranean Area. J Pediatr Gastroenterol Nutr 2017;64:e142-6.
13. Zhang SS, Yang J. Traditional Chinese medicine has great potential in the treatment of functional gastrointestinal disorders. World Chinese Journal of Digestology 2007;15:3457-61.
14. Wen YT, Xu ZH. Progress of clinical research on the treatment of pediatric stagnation with Chinese medicine. Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine 2024;(14):90-93+124.
15. Zou XQ, Ji XC, Huang XH, et al. Systematic review and meta-analysis of randomized controlled trials of the therapy of compound Chinese medicine in infantile dyspepsia. Journal of Yunnan University of Chinese Medicine 2020;(1):19-25.
16. Du Y, Wang QY, Cheng YM, et al. Summary of Wangshi Baochi pill for the treatment of digestive system disorders in patients with different ages. Shanghai Medical & Pharmaceutical Journal 2020;(13):36-8.
17. Gao T, Liu L, Wu Y, et al. Preclinical safety evaluation of WangShiBaoChiWan. Journal of Chinese Pharmaceutical Sciences 2022;31:31-46.
18. Center for Drug Evaluation, National Medical Products Administration. Technical guidelines for the preparation of drugs for clinical trials of new drugs of traditional Chinese medicine (trial) [EB/OL]. (2023-07-21) [2023-09-02]. Available online: https://www.cde.org.cn/main/news/viewInfoCommon/c36e5f39426b9a402be39c89016ebe7c
19. Xiao M, Ying J, Zhao Y, et al. Developing Placebos for Clinical Research in Traditional Chinese Medicine: Assessing Organoleptic Properties of Three Dosage Forms (Oral Liquid, Capsule and Granule). Front Pharmacol 2021;12:673729.
20. Tang XD, Bian LQ, Gao R, et al. Discussion on the preparation of placebo in clinical trials of Chinese herbal medicine. Chinese Journal of Integrated Traditional and Western Medicine 2009;29:656-8.
21. Hu SY, Ma R, Guang JX, et al. Treatment of functional dyspepsia in children with Wang shi Bao chi Pills: a randomized double-blind multicenter clinical trial. Chinese Journal of New Drugs 2019;28:179-83.
22. Wu SQ. Observation of curative effect of Wang's Baochi pill in the treatment of 110 cases of children with functional dyspepsia. Shanghai Medical & Pharmaceutical Journal 2018;(13):15-7.
23. Zhou YB, Wu M, Yan XJ, et al. Clinical study of Wangshi Baochi Pill on children with functional dyspepsia. China Journal of Traditional Chinese Medicine and Pharmacy 2014;29:3652-54.
24. Shi XR. Observation on the application of Wangshi Baochi Pills in children with anorexia due to dysfunction of spleen transportation. Xinjiang Journal of Traditional Chinese Medicine 2020;(5):27-8.
25. Xu QQ, Ni JX. Clinical report on the treatment of 144 cases of infantile anorexia with Wangshi Baochi Pills. Journal of Shaanxi University of Chinese Medicine 2000;(4):33.

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26. Tian S, Xue J, Song H, et al. Regulatory effects of traditional Chinese medicine on intestinal flora. Journal of Chinese Pharmaceutical Sciences 2020;29:161-75.
27. Wang AY, Lu J, Liu J, et al. Effects of "Wangshi Baochi Pill" on experimental spleen asthenia in mice. Shanghai Journal of Traditional Chinese Medicine 2004;(8):53-4.
28. Zhu Q. Research advances in gastrointestinal motility drugs and the development prospects of Wangshi Baochi Pills. Beijing Journal of Traditional Chinese Medicine 2000;(2):65.
29. Zhang QP, Zhang YP, Li CF, et al. Mechanism of Wangshi Baochi Pill in treating functional dyspepsia based on network pharmacology. Chinese Medicine Modern Distance Education of China 2020;(19):121-5.
30. Curien-Chotard M, Jantchou P. Natural history of gastroesophageal reflux in infancy: new data from a prospective cohort. BMC Pediatr 2020;20:152.
31. Wolke D, Bilgin A, Samara M. Systematic Review and Meta-Analysis: Fussing and Crying Durations and Prevalence of Colic in Infants. J Pediatr 2017;185:55-61.e4.

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