Postprint: Efficacy of Tiaozhong Yiqi Decoction in Treating Elderly Qi Deficiency-Type Slow Transit Constipation

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Abstract

Background The Tiaozhong Yiqi Decoction was originally used to treat gastrointestinal diseases caused by spleen deficiency and dampness stagnation. Years of clinical experience have revealed that modified Tiaozhong Yiqi Decoction can treat slow transit constipation (STC) in the elderly. Objective To evaluate the clinical efficacy of Tiaozhong Yiqi Decoction in treating elderly patients with qi-deficiency type slow transit constipation (STC) and its effect on intestinal motility. Methods A total of 100 patients with qi-deficiency type STC, diagnosed according to Traditional Chinese Medicine (TCM) criteria, were selected from the Anorectal Department and Preventive Treatment Center of Yinchuan Hospital of Traditional Chinese Medicine between May 2022 and April 2023. Using a 1:1 random number table method, patients were randomly divided into an observation group (n=50) and a control group (n=50). The observation group received oral administration of Tiaozhong Yiqi Decoction, while the control group received oral prucalopride succinate tablets, with each treatment lasting 4 weeks. Before treatment and after 4 weeks of treatment, records were made and comparisons were conducted regarding weekly complete spontaneous bowel movement (CSBM) scores, TCM syndrome scores, clinical symptom scores, and 48-hour and 72-hour marker excretion rates; gastrointestinal hormone levels were detected, and adverse reactions were observed. Results After 4 weeks of treatment, the observation group exhibited lower weekly CSBM scores, TCM syndrome scores, and various clinical symptom scores compared with the control group ($P<0.05$), along with higher 48-hour and 72-hour marker excretion rates ($P<0.05$). The observation group had lower serum levels of 5-hydroxytryptamine (5-HT), vasoactive intestinal peptide (VIP), and somatostatin (SS), while gastrin (GAS) was higher compared to the control group ($P<0.05$). After 4 weeks of treatment, the total clinical effective rate of the observation group was higher than that of the control group (2 =4.031, P=0.046); after 3 months of follow-up,

the recurrence rate of the observation group was lower than that of the control group (2 =5.134, P=0.023). During the study, 2 cases in the observation group experienced abdominal distension after taking Tiaozhong Yiqi Decoction, and 4 cases in the control group experienced dry mouth, nausea, dizziness, and other symptoms after taking prucalopride succinate tablets. No symptomatic treatment was administered, and symptoms resolved spontaneously after the trial concluded. Conclusion Tiaozhong Yiqi Decoction can improve TCM syndromes, gastrointestinal transit time, and clinical symptoms in elderly STC patients, regulate gastrointestinal neurohormone levels, promote gastrointestinal motility, and demonstrates a low clinical recurrence rate, making it worthy of clinical promotion.

Full Text

Efficacy of Tiaozhong Yiqi Decoction in Treating Elderly Qi-Deficiency Type Slow Transit Constipation

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Abstract

Background: Tiaozhong Yiqi Decoction was originally used to treat gastrointestinal diseases caused by spleen deficiency and dampness stagnation. Years of clinical experience have demonstrated that modified Tiaozhong Yiqi Decoction can effectively treat slow transit constipation (STC) in elderly patients.

Objective: To evaluate the clinical efficacy of Tiaozhong Yiqi Decoction in treating elderly qi-deficiency type STC and its effects on intestinal motility.

Methods: A total of 100 elderly patients with qi-deficiency type STC were selected from the Proctology Department and Preventive Treatment Center of Yinchuan Traditional Chinese Medicine Hospital between May 2022 and April 2023. Patients were randomly divided into an observation group (n=50) and a control group (n=50) using a 1:1 random number table method. The observation group received oral administration of Tiaozhong Yiqi Decoction, while the control group received oral Prucalopride Succinate tablets, with both groups treated for 4 weeks. Weekly complete spontaneous bowel movement (CSBM) scores, traditional Chinese medicine (TCM) syndrome scores, clinical symptom scores, and 48-hour and 72-hour marker excretion rates were recorded and compared before treatment and after 4 weeks of treatment. Gastrointestinal hormone levels were measured, and adverse reactions were monitored throughout the study period.

Results: After 4 weeks of treatment, the observation group demonstrated significantly lower weekly CSBM scores, TCM syndrome scores, and clinical symptom scores compared to the control group (P<0.05), along with higher 48-hour and 72-hour marker excretion rates (P<0.05). Serum levels of 5-hydroxytryptamine (5-HT), vasoactive intestinal peptide (VIP), and somatostatin (SS) were lower in the observation group, while gastrin (GAS) levels were higher (P<0.05). The total clinical effective rate in the observation group was significantly higher than in the control group after 4 weeks (2=4.031, P=0.046). During 3 months of follow-up, the recurrence rate in the observation group was significantly lower than in the control group (2=5.134, P=0.023). Two patients in the observation group experienced abdominal distension after taking Tiaozhong Yiqi Decoction, while four patients in the control group experienced dry mouth, nausea, and dizziness after taking Prucalopride Succinate tablets; none required symptomatic treatment, and all symptoms resolved spontaneously after trial completion.

Conclusion: Tiaozhong Yiqi Decoction can improve TCM syndromes, gastrointestinal transit time, and clinical symptoms in elderly STC patients, regulate gastrointestinal neurohormone levels, promote gastrointestinal motility, and maintain a low clinical recurrence rate, making it worthy of clinical promotion.

Keywords: Constipation; Slow transit constipation; Elderly; Qi-deficiency type; Prokinetic agents (TCM); Gastrointestinal hormones

Introduction

Elderly slow transit constipation (STC) has a complex etiology, primarily related to genetic factors, long-term medication use, lifestyle and dietary changes, and is closely associated with intestinal neuronal damage and abnormal neurotransmitter function, resulting in weakened gastrointestinal motility and slower food transit [1]. The condition is most common in patients over 60 years of age, with an incidence of approximately 18% that increases with age [2]. Chronic constipation not only seriously affects physical health but also causes psychological changes and may even induce cardiovascular and cerebrovascular events, creating significant life distress [3]. Current clinical treatments for STC primarily include oral prokinetic agents, various laxatives, and surgical intervention. While these approaches target specific pathological pathways and alleviate symptoms to some degree, they are prone to recurrence and ultimately increase patients' economic and psychological burden over time. This study investigates herbal formulas that can both promote qi movement and regulate qi stagnation based on extensive TCM clinical experience in treating chronic constipation. Drawing from the classical formula Tiaozhong Yiqi Decoction documented in *Lan Shi Mi Cang* (Secret Treasury of the Orchid Chamber) with appropriate modifications for elderly qi-deficiency type STC, this approach addresses the holistic integration of physical and mental health, comprehensively regulates abnormal

ascending and descending of qi in the five zang organs, focuses on tonifying the spleen and stomach in the middle jiao, and achieves the therapeutic goal of spleen ascending and stomach descending with harmonious organ qi—making it worthy of clinical application and promotion.

Methods

1.1 General Information

We prospectively selected 100 elderly patients with qi-deficiency type STC who visited the Proctology Department and Preventive Treatment Center (both outpatient and inpatient) of Yinchuan Traditional Chinese Medicine Hospital between May 2022 and April 2023. Using a 1:1 random number table method, patients were allocated to an observation group (n=50; 21 males, 29 females; age 60-75 years, mean 66.87$±4.92$years$; $diseasecourse$0.4-12.0$years$, $mean$5.36±2.84$years$)$and a control group ($n = 50; 23$males$, 27$females$; age61-74$years$, $mean$65.01±5.07$years$; $diseasecourse$0.5-11.6$years$, $mean$5.28±$3.14 years). The follow-up period was 3 months with a 100% follow-up rate. There were no statistically significant differences between the two groups in gender (2=0.687, P=0.162), age (t=-0.280, P=0.780), or disease course (Z=-0.301, P=0.764) (P>0.05). This study was approved by the Medical Ethics Committee of Yinchuan Traditional Chinese Medicine Hospital.

1.2 Diagnostic Criteria

1.2.1 Functional Constipation Criteria Functional constipation (FC) was diagnosed according to the Rome IV criteria [4], requiring symptom presence for $ $6 months with the following criteria met for the last 3 months: (1) Must include at least two of the following: straining during $ $25% of defecations; lumpy or hard stools in $ $25% of defecations; sensation of incomplete evacuation in $ $25% of defecations; sensation of anorectal obstruction/blockage in $ $25% of defecations; manual maneuvers to facilitate $ $25% of defecations; and spontaneous bowel movements <3 times per week. (2) Loose stools are rarely present without laxative use. (3) Does not meet criteria for irritable bowel syndrome. STC diagnosis was confirmed based on FC criteria combined with gastrointestinal transit time (GITT) examination demonstrating colonic motility dysfunction.

1.2.2 Qi-Deficiency Constipation Criteria Referring to the *Expert Consensus on TCM Diagnosis and Treatment of Constipation (2017)* [5], "qi-deficiency constipation" was defined by the following criteria. Main symptoms: (1) Weak defecation effort; (2) Dull abdominal pain with preference for pressure and rubbing; (3) Sweating and shortness of breath with straining. Secondary symptoms: (1) Fatigue after defecation; (2) Mental fatigue and reluctance to speak; (3) Poor appetite. Tongue and pulse: pale red tongue with thin

white coating, weak pulse. Diagnosis required all main symptoms plus any two secondary symptoms, combined with characteristic tongue and pulse findings.

1.3 Inclusion Criteria

(1) Met STC TCM syndrome differentiation and clinical diagnostic criteria; (2) Aged 60-75 years with no history of abdominal or pelvic surgery; (3) Mild to moderate condition; (4) No other constipation treatments (except emergency laxatives) in the past 2 weeks; (5) Good compliance and voluntary signed informed consent.

1.4 Exclusion Criteria

(1) Combined with severe cardiovascular, cerebrovascular, metabolic, digestive, psychological, cognitive disorders, or liver/kidney function impairment; (2) Outlet obstructive constipation, constipation-predominant irritable bowel syndrome, or organic gastrointestinal diseases; (3) Long-term use of antidepressants, opioid drugs, or alcohol abuse; (4) Allergy to trial medications; (5) Concealed medical history or poor compliance.

1.5 Dropout Criteria

(1) Patients voluntarily withdrew due to poor efficacy or adverse events preventing continued treatment; (2) Voluntary withdrawal of informed consent or loss to follow-up; (3) Failure to complete 80% of the treatment course and observation period; (4) Refusal of follow-up or provision of subjective efficacy data once during the trial; (5) Use of other defecation-assisting drugs unrelated to this trial during treatment.

1.6 Treatment Methods

Both groups adjusted lifestyle and bowel habits: daily dietary fiber intake >25g, water intake 1.5-2.0L, and appropriate exercise such as Baduanjin, Tai Chi, or walking. If patients did not defecate for >3 days during the trial, 800-1000mL of 0.9% sodium chloride solution could be used for a single cleansing enema to assist defecation.

Observation Group: Received Tiaozhong Yiqi Decoction [Astragalus membranaceus (raw) 30g, Cornus officinalis 10g, Bupleurum chinense (north) 10g, Cimicifuga racemosa 6g, Ziziphus jujuba var. spinosa seed 20g, Aucklandia lappa 10g, Atractylodes macrocephala (raw) 30g, Magnolia officinalis (ginger-processed) 20g, Fossilized dragon bone (decocted first) 20g, Anemarrhena asphodeloides 6g, Codonopsis pilosula 20g, Ligusticum chuanxiong 10g, Citrus reticulata peel 10g, Glycyrrhiza uralensis (honey-fried) 6g, Platycodon grandiflorus 10g]. Prepared uniformly by the hospital pharmacy department, each dose was divided into 3 bags of 200mL each, taken with warm water 1 hour after three daily meals.

Control Group: Received Prucalopride Succinate tablets (Shijiazhuang No. 4 Pharmaceutical Co., Ltd., batch number: H20203310), 2mg per dose, once daily, taken orally before meals.

Both groups received continuous treatment for 4 weeks.

1.7 Adverse Reactions

Adverse reactions (such as worsening abdominal pain, diarrhea, dizziness, headache, rash, etc.) were recorded truthfully during the study. Causes were analyzed based on severity, frequency, and duration, with timely symptomatic treatment provided when necessary.

1.8 Observation Indicators and Methods

Before treatment and after 4 weeks of treatment, the following were observed and recorded: complete spontaneous bowel movement (CSBM) frequency, TCM syndrome scores, gastrointestinal transit time (48-hour and 72-hour marker excretion rates), and clinical symptom scores. Both groups had gastrointestinal neurohormone levels [serum 5-hydroxytryptamine (5-HT), gastrin (GAS), vasoactive intestinal peptide (VIP), somatostatin (SS)] measured in the fasting state using ELISA before and after 4 weeks of treatment. Patient compliance was monitored, drug adverse reactions were recorded, and constipation recurrence rates were analyzed after 3 months of follow-up.

1.8.1 CSBM Scoring Standard CSBM/week $ $3 times: 0 points; 2 times/week $\leq$ CSBM/week <3 times: 1 point; 1 time/week $\leq$ CSBM <2 times: 2 points; CSBM <1 time/week: 3 points.

1.8.2 TCM Syndrome Scoring Using the TCM syndrome efficacy scoring table [6] to evaluate qi-deficiency constipation syndrome scores. Main symptoms: (1) Straining during defecation; (2) Dull abdominal pain with preference for pressure and rubbing; (3) Sweating and shortness of breath with straining. Secondary symptoms: (1) Fatigue after defecation; (2) Mental fatigue and reluctance to speak; (3) Poor appetite. Tongue and pulse: pale red tongue with thin white coating, weak pulse. Syndrome determination required all main symptoms plus 1-2 secondary symptoms. Main symptoms were scored 0, 2, 4, or 6 points based on severity; secondary symptoms were scored 0, 1, 2, or 3 points. Higher syndrome scores indicated more severe conditions.

1.8.3 Gastrointestinal Transit Time Laxatives, suppositories, and enemas were discontinued 5 days before examination. On the examination day at 8:00 AM, patients ingested one capsule containing 24 radiopaque gastrointestinal motility markers (Kaiser Pharmaceuticals, USA, batch number: E22401). Abdominal X-rays were taken at 8:00 AM at 48 and 72 hours after capsule ingestion. The number of residual markers in the intestine was observed and counted to

calculate the excretion rate. A 72-hour excretion rate $ $80% was considered negative.

1.8.4 Gastrointestinal Neurohormone Measurement Under fasting conditions, 3-5mL of venous blood was drawn from patients and centrifuged at 3000 r/min with an 8cm radius for 10 minutes to separate serum, which was stored at -30°C. Levels of 5-HT, GAS, VIP, and SS were measured.

1.8.5 Clinical Symptom Scoring Standards

(1) Defecation urge score: none = 3 points; occasional = 2 points; sometimes = 1 point; often = 0 points. (2) Stool form score: Based on Bristol Stool Form Scale–Type I (nut-like hard lumps) = 5 points; Type II (hard sausage-shaped) = 4 points; Type III (sausage-shaped with cracks) = 3 points; Type IV (soft sausage-shaped) = 2 points; Type V (soft blobs) = 1 point. (3) Defecation duration score: <5 min = 0 points; 6-10 min = 1 point; 11-20 min = 2 points; 21-30 min = 3 points; >30 min = 4 points. (4) Symptom scores for weak defecation, incomplete evacuation, abdominal distension, etc.: none = 0 points; mild = 1 point; obvious = 2 points; severe = 3 points.

1.8.6 Efficacy Criteria Referring to the *Chinese Expert Consensus on Chronic Constipation (2019, Guangzhou)* [7] and GITT, efficacy criteria after 4 weeks of treatment were established. Cured: constipation symptoms disappeared, CSBM/week $ $3 times, 72-hour marker excretion rate $ $80%. Markedly effective: constipation symptoms significantly improved, 2 ≤ CSBM/week <3 times, 60% ≤ 72-hour marker excretion rate <80%. Effective: constipation symptoms improved, CSBM/week <2 times, 40% ≤ 72-hour marker excretion rate <60%. Ineffective: no change in constipation symptoms, CSBM/week, or 72-hour marker excretion rate. Total effective rate = (cured + markedly effective + effective) / total cases × 100%.

1.9 Statistical Methods

SPSS 24.0 software was used for statistical analysis. Measurement data were expressed as ($\bar{x}\pm s$). Two independent samples t-test was used for normally distributed data, and Mann-Whitney U test for non-normally distributed data. Count data were described using relative numbers and analyzed with 2 test. All statistical tests were two-sided, with P<0.05 considered statistically significant.

Results

2.1 Comparison of Weekly CSBM Scores, TCM Syndrome Scores, and Marker Excretion Rates

After 4 weeks of treatment, the observation group showed statistically significant differences in weekly CSBM scores, TCM syndrome scores, and 48-hour and 72-hour excretion rates compared to baseline ($P<0.05$). The control group also demonstrated reduced weekly CSBM scores and increased 48-hour and 72-hour excretion rates compared to baseline ($P<0.05$). Following 4 weeks of treatment, the observation group had superior weekly CSBM scores, TCM syndrome scores, and 48-hour and 72-hour excretion rates compared to the control group, with statistically significant differences ($P<0.05$), see Table 1 .

2.2 Comparison of Gastrointestinal Neurohormone Levels

After 4 weeks of treatment, serum 5-HT and GAS levels in the observation group were higher than baseline, while VIP and SS levels were lower, with statistically significant differences ($P<0.05$). In the control group, VIP and SS decreased while 5-HT increased compared to baseline, all showing statistically significant differences ($P<0.05$). After 4 weeks of treatment, the observation group had higher GAS levels but lower 5-HT, VIP, and SS levels compared to the control group, with statistically significant differences ($P<0.05$), see Table 2 .

2.3 Comparison of Clinical Symptom Scores

After 4 weeks of treatment, the observation group had lower scores for defecation urge, stool form, defecation duration, incomplete evacuation, weak defecation, and abdominal distension compared to baseline ($P<0.05$). The control group showed lower scores in all items except stool form and weak defecation compared to baseline ($P<0.05$). After 4 weeks of treatment, all clinical symptom scores in the observation group were lower than those in the control group, with statistically significant differences ($P<0.05$), see Table 3 .

2.4 Comparison of Clinical Efficacy and 3-Month Recurrence Rate

After 4 weeks of treatment, the total clinical effective rate in the observation group was higher than in the control group (2=4.031, P=0.046). During 3 months of follow-up, the recurrence rate in the observation group was lower than in the control group, with statistically significant difference (2=5.134, P=0.023), see Table 4 .

2.5 Compliance and Adverse Reactions

No patients were lost to follow-up during the study. Two patients in the observation group experienced abdominal distension after taking Tiaozhong Yiqi Decoction, while four patients in the control group experienced dry mouth, nausea, and dizziness after taking Prucalopride Succinate tablets. None required

symptomatic treatment, and all symptoms resolved spontaneously after trial completion.

Discussion

The *Suwen · Yinyang Yingxiang Dalun* states: "At age sixty, yin and qi greatly decline, the nine orifices become unfavorable, lower deficiency and upper excess occur, and tears and nasal discharge appear." This illustrates that at age sixty, the body' s qi, blood, body fluids, and organ functions gradually decline, the five zang organs and six fu organs lose nourishment, yin and yang become deficient—especially lung, spleen, and kidney functions—leading to unfavorable nine orifices, including impaired large intestine function in transmitting waste and resulting in difficult defecation. The authors believe that elderly STC is related to all five zang organs, with pathological characteristics of mixed qi, blood, phlegm, dampness, fire, and other pathological factors, with both deficiency and excess coexisting. The disease location is in the large intestine, closely related to the lung, spleen, and kidney, and involving the heart and liver. Treatment should focus on raising clear qi and descending turbid qi, regulating and tonifying middle qi, enabling clear yang to ascend and turbid yin to descend naturally, emphasizing dredging of triple burner qi movement, with the key being regulation of lung, spleen, and kidney qi movement.

This study employed a self-formulated Tiaozhong Yiqi Decoction to treat elderly STC. In the formula, *Atractylodes macrocephala* (raw) is sweet, bitter, and warm —an essential herb for warming the spleen and assisting transportation. Recent research demonstrates that raw *Atractylodes* water extract can effectively improve fecal water content, 12-hour fecal pellet count, and small intestine propulsion rate in rats ($P<0.01$), while its polysaccharides significantly increase plasma motilin (MTL) levels ($P<0.001$) and decrease VIP levels ($P<0.001$) in constipated rats [8]. *Astragalus membranaceus* is sweet and warm, excellent at tonifying middle qi, raising clear yang, and generating fluid while controlling bleeding. Shi et al. [9] employed network pharmacology and molecular docking to identify 20 compounds in *Astragalus* acting on 143 targets related to STC, treating the condition through multi-target, multi-pathway synergy. The formula heavily uses raw *Astragalus* and raw *Atractylodes* as sovereign drugs to strengthen the spleen, restore body fluids, generate qi and blood, and move the middle jiao without causing dryness. *Codonopsis pilosula* tonifies middle qi and generates fluids; *Magnolia officinalis* dries dampness, transforms phlegm, and descends qi to widen the intestines. Zhang et al. [10], based on the "lung and large intestine are interior-exteriorly related" theory, used a self-formulated qi-tonifying and spleen-strengthening decoction to treat STC, which inhibited synthesis of VIP and SS in gastrointestinal neurotransmitters, increased substance P (SP) secretion, restored normal intestinal smooth muscle contraction and relaxation, promoted gastrointestinal peristalsis, and improved constipation symptoms, achieving a clinical effective rate of 95.35%. Research has found that

Magnolia can significantly improve gastrointestinal motility disorders in control rats, enhance gastric absorption and small intestine propulsion ($P<0.001$) [11], with mechanisms involving enhanced gastrointestinal motility through increased L-tryptophan and 5-HT levels in the tryptophan pathway. Fossilized dragon bone and *Ziziphus jujuba* var. *spinosa* seed calm the mind and anchor liver yang, serving as minister herbs that both tonify and dredge, eliminating hyperactive liver yang, providing heart support, and pacifying the five zang organs. For functional gastrointestinal diseases, studies show that using calming herbs such as fossilized dragon bone, lily, and *Ziziphus jujuba* var. *spinosa* seed can increase the clinical total effective rate to 72.94% [12-13].

Bupleurum chinense is the guiding herb for Shaoyang, directing sinking atmospheric qi to ascend from the left; *Cimicifuga racemosa* is a Yangming herb, directing sinking atmospheric qi to ascend from the right while nourishing heart qi; *Platycodon grandiflorus* carries the effects of various herbs upward to the chest, combined with *Astragalus* to raise sinking middle qi. Scholars using data mining and association rule analysis of ancient and modern famous physicians' herbal prescriptions for functional constipation found that among spleen-strengthening and qi-tonifying herbs, *Bupleurum*, *Platycodon*, and *Cimicifuga* were frequently used and served as core herbal pairs, thereby restoring spleen transportation, enabling clear qi to ascend, and unblocking the lower jiao [14-15]. *Cornus officinalis* effectively tonifies liver and kidney, benefiting both essence and yang, combined with dragon bone to restrain qi consumption; *Anemarrhena asphodeloides* prevents yang qi from accumulating and generating heat, providing cool moistening balance. Li et al. [16] used data mining to study prescription patterns in *Jingyue Quanshu* for treating constipation, extracting 45 formulas and 84 herbs, among which tonifying deficiency herbs were used 132 times (44.90%), heat-clearing herbs 31 times (10.54%), with *Cornus* used 7 times and *Anemarrhena* 5 times. *Ligusticum chuanxiong*, *Aucklandia lappa*, and *Citrus reticulata* peel are aromatic stomachics that regulate lung and spleen qi ascending and descending to regulate middle qi, while also drying dampness and regulating qi to transform phlegm as adjuvant herbs. Research found that *Citrus reticulata* peel-*Aucklandia lappa* volatile oil participates in neuroactive ligand-receptor interactions, AGEs-RAGE and Ca2+ signaling pathways, endocrine resistance, and other multi-target, multi-pathway mechanisms to treat constipation [17]. *Glycyrrhiza uralensis* (honey-fried) tonifies qi, supplements middle, and harmonizes all herbs as the envoy drug. The entire formula tonifies qi and assists transportation, combines ascending and descending, and promotes smooth defecation.

After 4 weeks of treatment, the observation group demonstrated higher CSBM/week, 48-hour and 72-hour excretion rate scores, and lower qi-deficiency STC TCM syndrome scores and clinical symptoms compared to the control group, with statistically significant differences ($P<0.05$). These results indicate that oral Tiaozhong Yiqi Decoction significantly increased weekly defecation frequency in elderly patients compared to the control group, demonstrating that the decoction promotes gastrointestinal peristalsis, improves intestinal

transit function, promotes fecal excretion, helps correct patients' qi-deficiency constitution, restores intestinal motility, and relieves clinical discomfort. Tiaozhong Yiqi Decoction also increased 48-hour and 72-hour marker excretion rates, confirming that GITT can indeed evaluate intestinal transit motility and serve as an important objective indicator for defecation disorders. Furthermore, after 4 weeks of treatment, the total effective rate in the observation group was higher than in the control group ($P<0.05$), and 3-month follow-up showed a lower recurrence rate in the observation group ($P<0.05$), indicating that the observation group achieved relatively stable medium-term efficacy, could maintain a relatively stable health state in patients for medium to long term, and helped relieve patients' psychological stress.

Research demonstrates that enteric nervous system (ENS), interstitial cells of Cajal, and colonic smooth muscle dysfunction are major factors causing STC [18]. When ENS distributed in the submucosa releases gastrointestinal neurotransmitters and various hormones in disorder, or becomes insensitive to food and drug stimuli, it affects gastrointestinal motility [19]. Its neurotransmitters are divided into excitatory neurotransmitters (5-HT, GAS) that promote gastrointestinal smooth muscle contraction, and inhibitory neurotransmitters (VIP, SS) that inhibit gastrointestinal peristalsis and emptying. These neurotransmitters mutually restrict each other to maintain dynamic balance. GAS is produced by G cells, promotes gastric acid and pancreatic digestive enzyme secretion, similar to motilin, excites smooth muscle contraction, and promotes gastrointestinal motility [20]. 5-HT is widely distributed in gastrointestinal tissue and stimulates gastrointestinal peristalsis by promoting acetylcholine release. It binds to different specific receptors to produce different gastrointestinal effects, with 5-HT3 and 5-HT4 receptors being most studied. 5-HT4R is a G protein-coupled receptor in enteric neurons, intestinal epithelial cells, and intestinal smooth muscle cells that, when activated, promotes intestinal smooth muscle peristalsis, increases digestive fluid secretion, improves stool form, and promotes excretion [21]. Prucalopride is a high-affinity 5-HT4R agonist widely used clinically. VIP exists in colonic nerve plexuses, primarily relaxing the esophagus, gastrointestinal tract, and internal anal sphincter, delaying gastric emptying, inhibiting intestinal movement, and suppressing secretion of pancreatic juice, intestinal fluid, electrolytes, and GAS [22]. SS is not only a neurohormone and neurotransmitter but also a gastrointestinal hormone, most abundant in the gastrointestinal tract, inhibiting intestinal peristalsis, reducing intestinal fluid and some polypeptide hormone secretion, and decreasing intestinal blood flow [23]. Before treatment, serum SS and VIP levels were elevated while 5-HT and GAS levels were low. After 4 weeks of treatment, serum SS and VIP scores in the observation group decreased compared to the control group ($P<0.05$), while 5-HT and GAS scores increased ($P<0.05$), indicating that the formula effectively promoted gastrointestinal peristalsis, gastric emptying, and increased gastrointestinal fluid secretion by rebalancing these four gastrointestinal neurotransmitters, thereby improving stool form, shortening defecation time, increasing defecation urge, and relieving symptoms of incomplete evacuation, weak defecation, and

abdominal distension. These effects may be achieved by regulating ENS conduction and gastrointestinal smooth muscle.

In summary, Tiaozhong Yiqi Decoction can alleviate constipation clinical symptoms, improve TCM syndromes, increase defecation frequency, and promote intestinal peristalsis in qi-deficiency patients by regulating and tonifying the lung, spleen, and kidney, possibly by adjusting disordered gastrointestinal hormone levels. Moreover, it demonstrates high clinical cure rate and low recurrence rate, with good medium to long-term efficacy, achieving the therapeutic goal for STC with long-term treatment. However, this study has a short cycle and limited sample size, and still lacks objective indicators. Future research should further optimize and improve the prescription for qi-deficiency constipation, deeply explore the mechanism of Tiaozhong Yiqi Decoction in treating STC, and benefit more patients.

Author Contributions

Zhao Hongbo conceived the research idea, wrote the article, and was responsible for the overall paper. Fan Xianxian, Wang Hongwei, and Zhao Lan were responsible for clinical trial implementation, specimen collection, and case follow-up. Yang Yun and Ge Zhiming were responsible for data collection, summarization, and collation. Wu Xiaojing was responsible for statistical analysis and table preparation.

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Tables

Table 1 Comparison of weekly CSBM scores, TCM syndrome scores, and marker excretion rates between the two groups ($\bar{x}\pm s$, points)

Table 2 Comparison of gastrointestinal neurohormone levels between the two groups ($\bar{x}\pm s$)

Table 3 Comparison of clinical symptom scores of constipation between the two groups ($\bar{x}\pm s$)

Table 4 Comparison of clinical efficacy between the two groups of patients [n (%)]

Note: In all tables, superscript "a" indicates P<0.05 compared to baseline, and superscript "b" indicates P<0.05 compared to the control group after 4 weeks of treatment.

Note: Figure translations are in progress. See original paper for figures.