

Effect of Modified Wendan Decoction on Serological Indices and Safety Analysis in Elderly with Chronic Cholecystitis of Damp-Heat Syndrome in Liver and Gallbladder

JING HAN, JINGCHAO CHEN¹, MENG ZHU, ZHANG HUI² AND SHAOHONG HU*

Department of Emergency, Changchun Traditional Chinese Medicine Hospital, ¹Third Affiliated Clinical Hospital of Changchun University of Traditional Chinese Medicine, ²Department of Hepatology, Changchun Traditional Chinese Medicine Hospital, Changchun, Jilin Province 130000, China

Han *et al.*: Effect of Modified Wendan Decoction on Serological Indicators in Elderly

To observe the effect of modified Wendan decoction on serological indicators in elderly patients with chronic cholecystitis of damp-heat syndrome in liver and gallbladder, and to evaluate the safety of this treatment regimen. A total of 60 elderly patients with chronic cholecystitis of damp-heat syndrome in liver and gallbladder admitted to our hospital from March 1st 2024 to May 31st 2024 were selected and evenly assigned to the control group (n=30) and the observation group (n=30) using the envelope method. The control group was treated with anti-inflammatory and gallbladder-stimulating tablets, while the observation group received modified Wendan decoction in addition to the treatment given to the control group. Each course of treatment lasted for 2 w, and both groups were treated for 2 courses. After the 2 courses, changes in serum inflammatory factor levels and immune function indices were observed in both groups. The comprehensive efficacy and safety of the two groups were evaluated based on the traditional Chinese medicine syndrome scores and color Doppler ultrasonography findings. After receiving 2 courses of treatment, the treatment regimen combining modified Wendan decoction and anti-inflammatory and gallbladder-stimulating tablets could effectively alleviate clinical symptoms, improve gallbladder function, and significantly enhance the clinical comprehensive efficacy. This treatment regimen did not cause significant damage to liver and kidney function, had high safety, and could control the inflammatory response in patients with chronic cholecystitis, providing an effective conservative treatment option for elderly patients with chronic cholecystitis of damp-heat syndrome in liver and gallbladder.

Key words: Wendan decoction, chronic cholecystitis, damp-heat syndrome, liver, gallbladder, serological indicators

Chronic cholecystitis is a common clinical disease, with a peak incidence in China among individuals aged 50 and above. The prevalence rate in the 60 y-69 y age group is 8.3 %, and it reaches a high of 11.2 % in individuals aged 70 y and above. Due to changes in dietary structure and lifestyle among the Chinese population, the incidence of chronic cholecystitis is expected to continue rising in the next decade^[1]. Existing clinical studies indicate that the prevalence of chronic cholecystitis in China is positively correlated with increasing age^[2,3]. Among the elderly, natural physiological aging and decreased organ function lead to a reduction in physical activity, exacerbating the accumulation of lipids in the body, resulting in a higher incidence of gallbladder diseases

in this age group. The clinical manifestations of chronic cholecystitis vary greatly. According to the research by Sun *et al.*^[4], approximately 70 % of patients with chronic cholecystitis are asymptomatic, and clinical treatment should be individualized based on whether the patient has clinical symptoms and comorbidities. Due to the decline in physiological functions among the elderly, their recovery ability is also reduced, and some elderly patients often have comorbidities such as diabetes, respiratory disorders, and cardiovascular and cerebrovascular diseases. In China, 57.4 % of elderly patients have comorbidities such as hypertension and coronary heart disease, which increase the difficulty of treatment^[5].

*Address for correspondence
E-mail: 307600081@qq.com

The conventional treatments for chronic cholecystitis include surgery, medication, and general measures. However, research by Peng *et al.*^[6] showed that 27.03 % of patients had a low quality of life after gallbladder removal surgery. There is a lack of high-quality clinical evidence regarding whether elderly patients with asymptomatic chronic cholecystitis can benefit from preventive surgical treatment. Cholecystitis falls under the category of gallbladder distension, rib pain, and jaundice in Traditional Chinese Medicine (TCM). According to TCM theory, this disease is caused by external pathogenic factors such as dampness and heat, coupled with the patient's excessive consumption of fatty, sweet, and spicy foods, irregular diet, and accumulation of dampness and heat in the liver and gallbladder, leading to internal heat generation, obstruction of the liver and gallbladder, and eventual pathogenesis^[7]. Chinese medicine has rich theoretical and clinical experience in treating chronic cholecystitis. Although the etiology and pathogenesis of chronic cholecystitis are complex and variable, Chinese medicine treatment prioritizes clarifying the etiology and treating the root cause of the disease. In terms of treatment strategies, it adopts a combination of soothing the liver and regulating qi, clearing heat, and removing dampness^[8]. Research by Luan *et al.*^[9] showed that Chinese medicine can control the levels of inflammatory factors and reduce the expression of immune mediators in patients with chronic cholecystitis, demonstrating good clinical efficacy. Based on this, the present study used the modified Wendan decoction to treat elderly patients with chronic cholecystitis of damp-heat syndrome of the liver and gallbladder, providing a safer and

more effective method for clinical treatment of such patients.

MATERIALS AND METHODS

General information:

This study is a prospective study aiming to select elderly patients with chronic cholecystitis of damp-heat syndrome of the liver and gallbladder who visited the outpatient clinic of our hospital from March 1st 2024, to May 31st 2024, as the research subjects. A total of 60 patients were ultimately included and were equally assigned to the control group (n=30) and the observation group (n=30) using the envelope method. The baseline characteristics of the two groups were comparable ($p>0.05$). See Table 1 for details. This study has obtained approval from the hospital ethics committee.

Diagnostic criteria:

Western medicine diagnosis criteria: Based on the internal medicine^[10]. Patients exhibit persistent and recurrent distending pain or discomfort in the right upper abdomen, which may radiate to the scapular region. Patients have definite digestive system symptoms, which worsen after consuming fatty foods. The condition has a prolonged duration, with recurring clinical symptoms that manifest as a periodic pattern of acute attacks and remission. Examination reveals tenderness or percussion tenderness in the gallbladder region. B-ultrasound examination indicates gallbladder pathology. Imaging suggests pathological changes in the gallbladder. A definitive diagnosis can be made if any one of the conditions is met, along with any two of the conditions.

TABLE 1: COMPARISON OF BASELINE DATA BETWEEN THE TWO PATIENT GROUPS (n=60)

Baseline data	Control group (n=30)	Experimental group (n=30)	t/ χ^2	p
Age	60-72	59-71		
Average age (years)	66.03±5.11	65.42±5.42	0.449	0.655
Gender			0.071	0.791
Male	19 (63.33)	18 (60.00)		
Female	11 (36.67)	12 (40.00)		
Average disease duration (years)	1.40±0.25	1.34±0.26	0.911	0.366
Average body mass index (kg/m ²)	23.06±2.53	23.32±3.49	0.33	0.742

Chinese medicine disease diagnosis: Referring to the guiding principles for clinical research of new Chinese medicines^[11]. Main symptoms include discomfort in the right rib region. Secondary symptoms include dry mouth and bitter taste, nausea and vomiting, abdominal distension, reduced appetite, etc.

Chinese medicine syndrome diagnosis: Referring to the consensus opinions on expert diagnosis and treatment of cholecystitis in Chinese medicine^[12].

Liver and gallbladder damp-heat syndrome:

Main symptoms: Distending pain in the ribs and sides; bitter taste in the mouth upon waking; dry mouth and desire to drink.

Secondary symptoms: Yellowing of the skin and eyes; body heaviness and fatigue; abdominal distension and fullness; dry throat; short and yellow urine and uncomfortable or constipated bowel movements.

Tongue and pulse: Red tongue with yellow or thick greasy fur; slippery and rapid pulse.

Immediate diagnosis is made if one main symptom and three secondary symptoms are present.

Inclusion criteria:

Age range from 55 y to 75 y, gender not limited and meets the diagnostic criteria of both Western and Chinese medicine. Cultural, social background and occupational factors are not specifically limited. Each participant has a full understanding and awareness of the study, has undergone a formal informed consent process, and signed the informed consent form.

Exclusion criteria:

Patients in an acute phase of the disease or with a recent (within 1 w) history of acute onset; concomitant with other digestive system diseases; those who have taken medication or received treatments that may affect the accuracy of the study results before the start of the study; other pathological or physiological conditions that may affect the study's observation indicators. Severe liver and kidney dysfunction and history of previous mental illness were excluded from this study

Withdrawal criteria:

Not meeting the inclusion criteria or errors occurring during the inclusion process; lack of completeness

in clinical data; severe adverse reactions (included in adverse reaction statistics); participants who take other medications due to special conditions during treatment. For those patients whose efficacy has been clearly demonstrated at the time of withdrawal or dropout, their data will be included in the evaluation of therapeutic efficacy.

Methods:

Control group: The patients received anti-inflammatory and gallbladder-clearing tablets (manufactured by Guangdong Luofushan Pharmaceutical Co., Ltd., National Drug approval No: Z44021422). The dosage was 6 tablets per time, 3 times per day. A treatment cycle lasted for 2 w, and the patients were treated for 2 consecutive cycles.

Observation group: Based on the treatment mentioned above, the patients received modified Wendanxia decoction, which consisted of *Pinellia ternata* (Banxia) 15 g, *Astragalus membranaceus* (Huangqi) 10 g, *Paeonia lactiflora* (Baishao) 10 g, dried Tangerine Peel (Chenpi) 12 g, Licorice root (Gancao) 15 g, *Aurantii fructus* (Zhike) 15 g, *Poria cocos* (Fuling) 10 g, and *Bupleurum chinense* DC and (Chaihu) 15 g. If the patient had significant abdominal discomfort, additional Qingpi (*Citrus reticulata* Blanco var. *poonensis*) 10 g and *Cyperus rotundus* (Xiangfu) 10 g were added. If the patient had sediment-like gallstones, additional *Lysimachia christinae* Hance (Jinqiancao) 15 g and *Gallus domesticus* Brisson (Jineijin) 15 g were included in the main formula. For patients with frequent eructation, *Melia toosendan* Sieb., and *Zucc.* (Chuanlianzi) 15 g and *Curcuma aromatica* Salisb. (Yujin) 15 g were added. All the herbal medicines were decocted in water, with one dose per day. After decoction, the resulting juice was kept to 150 ml, and 50 ml was taken orally three times a day. A treatment cycle lasted for 2 w, and the patients were treated for 2 consecutive cycles.

Observation indicators:

TCM syndrome scores: According to the guiding principles for clinical research of new Chinese medicines (Trial Version)^[11] and the consensus opinion on TCM diagnosis and treatment of cholecystitis^[12], TCM syndrome scores were evaluated for both groups before and after treatment. The main symptoms included upper abdominal pain (scored as 2 points if the pain Visual Analog Scale (VAS) ≤ 3 ; 4 points if >3 and ≤ 7 ; 6 points if

>7), frequent nausea and vomiting (scored as 2 points for occasional occurrence with self-relief; 4 points for frequent occurrence but temporary relief with rest or medication; 6 points for persistent and unrelieved symptoms), dryness and bitterness in the mouth (scored similarly as nausea and vomiting), and discomfort on both sides of the chest (scored similarly as nausea and vomiting).

Imaging efficacy: Upper abdominal ultrasonography (Kunlun Resona R9 color Doppler ultrasound diagnostic instrument, Mindray Medical International Co., Ltd., Shenzhen, China) was used to observe changes in gallbladder imaging before and after treatment, and evaluate the imaging efficacy of both groups. The total effective rate of imaging efficacy was calculated as (number of cured cases+number of effective cases)/total number of cases \times 100 %.

Comprehensive efficacy: The comprehensive efficacy of both groups was evaluated based on TCM syndrome scores and imaging results. The total effective rate of comprehensive efficacy was calculated as the sum of cure rate, marked improvement rate, and effective rate.

Safety evaluation: Adverse reactions during the diagnosis and treatment process in both groups were observed and recorded in detail to evaluate the safety performance of the treatments received by these two groups.

Serological indicators: Serum levels of Interleukin (IL)-6, IL-8, Tumor Necrosis Factor-Alpha (TNF- α), and C-Reactive Protein (CRP) as well as immune function indicators such as serum Immunoglobulin A (IgA), Immunoglobulin G (IgG), and Immunoglobulin M (IgM) were observed in both groups before treatment and after two treatment courses. 5 ml of fasting venous blood was collected from patients before and after treatment, centrifuged (3000 r/min, 20 min) to separate serum, aliquoted, and stored at -40° for later measurement. A DR-200Bn microplate reader (Wuxi Hwaweidulang Instrument Co., Ltd.) was used to measure serum indicators, and the operation was strictly performed according to the instructions of the reagent kit, which was purchased from Wuhan Saipei Biotechnology Co., Ltd.

Gastrointestinal hormones: 5 ml of fasting venous blood was collected from both groups before treatment and after two treatment courses. After routine centrifugation, Enzyme-Linked Immunosorbent Assay (ELISA) was used to observe the levels of Motilin (MTL) and Gastrin (GAS) in

both groups.

Criteria for evaluating therapeutic effects:

The criteria for evaluating therapeutic effects were established based on the guiding principles for clinical research of new Chinese medicines (Trial Version)^[11] and the consensus opinion on TCM diagnosis and treatment of cholecystitis^[12].

Criteria for imaging therapeutic effects: The therapeutic effects were evaluated based on three major imaging data; the reduction in gallbladder volume, changes in gallbladder wall thickness, and changes in gallbladder wall morphology. Specifically, cure refers to the regression of all imaging indicators to normal ranges; marked effectiveness refers to significant improvement in two or more imaging indicators after treatment; effectiveness refers to improvement in only one imaging indicator and ineffectiveness refers to no significant improvement or even deterioration in gallbladder imaging after treatment.

Criteria for evaluating comprehensive therapeutic effects: In cure; the TCM syndrome score of the patient has significantly decreased by >90 % and imaging examinations also confirm that the physiological status has returned to normal levels. In marked effectiveness; during the entire treatment process, the TCM syndrome score of the patient has decreased by >70 % compared to before, and imaging examinations also meet the criteria for marked effectiveness. In effectiveness; compared to before treatment, the TCM syndrome score of the patient has decreased by at least 30 % and imaging examination results also meet the criteria for effectiveness. If the TCM syndrome score of the patient has only slightly decreased by <30 % and no significant improvement is observed in imaging examinations, the treatment will be considered ineffective.

Safety evaluation indicators: General vital signs observation, including changes in body temperature, heart rate, respiration and blood pressure during treatment. Newly developed symptoms and signs during treatment including rash, fever, diarrhea, nausea, vomiting and anorexia. Safety tests, including the detection of liver and kidney function indicators in both groups before and after treatment to observe whether the drugs used have hepatorenal toxicity. Whether the patient adheres to the doctor's advice in taking medication and whether the patient takes other medications that may interfere with the

accuracy of the study results during the study period.

Statistical methods:

All data obtained in this study were analyzed using Statistical Package for the Social Sciences (SPSS) 23.0 statistical software. Measurement data were expressed as (mean±standard deviation) and evaluated using the t-test. Counting data were tested using the Chi-square (χ^2) test. Ranked data were analyzed using the Mann-Whitney U test to ensure the accuracy of the results. A $p < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

There was no statistical difference in the quantitative scores of TCM symptoms between the two groups before treatment (17.68±2.03) points vs. (17.91±2.53) points, ($t=0.388$, $p=0.699$). After treatment, the quantitative scores of TCM symptoms in the observation group were significantly lower than those in the control group during the same period ((2.74±0.88) points vs. (8.32±2.09) points, $t=13.477$, $p < 0.01$) as shown in Table 2.

The imaging therapeutic effect in the observation group was superior to that in the control group (96.67 % vs. 70.00 %, $z=2.102$, $p < 0.05$) as shown in Table 3.

The comprehensive therapeutic effect in the observation group was significantly better than that in the control group (96.67 % vs. 73.33 %, $z=3.235$, $p < 0.01$) as shown in Table 4.

All 60 patients participating in the clinical study completed the treatment strictly according to the

doctor's instructions during the treatment period. No patients were found to have taken other medications privately that could affect the accuracy of the study results. There were no abnormalities in liver and kidney function tests before and after treatment in both groups. Basic vital signs remained stable during medication. No hepatorenal toxicity was observed in the clinical application of Xiaoyan Lidan Pian (a TCM for treating gallbladder inflammation) and Wendan Tang Jiajian (a modified TCM formula). During the study, a total of 2 patients in the observation group exhibited adverse reactions, while no significant adverse reactions were observed in the control group. There was no statistically significant difference in the incidence of adverse reactions between the two groups during medication (6.67 % vs. 0 %, $\chi^2=2.069$, $p=0.150$) as shown in Table 5.

After two courses of treatment, the levels of IL-8, TNF- α and CRP in both groups were lower than those before treatment ($p < 0.05$), and the levels of IL-8, TNF- α , and CRP in the observation group were lower than those in the control group during the same period ($p < 0.05$). There was no statistically significant difference in the levels of IgA, IgG, and IgM before and after treatment in both groups ($p > 0.05$) as shown in Table 6 and Table 7.

Before treatment, there was no statistical difference in gastrointestinal hormone indicators between the two groups ($p > 0.05$). After treatment, both MTL and GAS levels increased compared to the previous levels, and the improvement in the observation group was superior to that in the control group during the same period ($p < 0.05$) as shown in Table 8.

TABLE 2: COMPARISON OF QUANTIFIED SCORES OF TCM SYMPTOMS BEFORE AND AFTER TREATMENT IN THE TWO PATIENT GROUPS ($\bar{x} \pm s$, score)

Group	Number of cases	Before treatment	After 2 courses of treatment
Observation	30	17.68±2.03	2.74±0.88*
Control	30	17.91±2.53	8.32±2.09*
t		0.388	13.477
p		0.699	<0.001

Note: Compared with before treatment in the same group, * $p < 0.05$

TABLE 3: COMPARISON OF IMAGING THERAPEUTIC EFFECTS BETWEEN THE TWO PATIENT GROUPS (n, %)

Group	Number of cases	Cured	Effective	Ineffective	Total effective rate
Observation	30	2	27	1	96.67
Control	30	0	21	9	70.00
z	2.102	0.388	0.388	0.388	0.388
p			0.036		

TABLE 4: COMPARISON OF COMPREHENSIVE THERAPEUTIC EFFECTS BETWEEN THE TWO PATIENT GROUPS (n, %)

Group	Number of cases	Cured	Marked effect	Effective	Ineffective	Total effective rate
Observation	30	10	13	6	1	96.67
Control	30	4	6	12	8	73.33
z				3.235		
p				0.001		

TABLE 5: COMPARISON OF SAFETY PROFILES BETWEEN THE TWO PATIENT GROUPS (n, %)

Group	Number of cases	Abnormalities in liver and kidney function	Abnormalities in basic vital signs	Skin rash	Gastrointestinal reaction	Fever	Total incidence rate
Observation	30	0	0	1	0	1	6.67
Control	30	0	0	0	0	0	0
χ^2				2.069			
p				0.150			

TABLE 6: COMPARISON OF SEROLOGICAL INDICES BEFORE AND AFTER TREATMENT IN THE TWO GROUPS ($\bar{x}\pm s$)

Group	Number of cases	IL-8 (pg/ml)		TNF- α (pg/ml)		CRP (mg/l)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation	30	49.68 \pm 15.32	26.93 \pm 8.45*	60.29 \pm 8.55	37.29 \pm 6.34*	40.74 \pm 6.94	20.26 \pm 4.35*
Control	30	49.63 \pm 15.18	32.83 \pm 10.47*	59.48 \pm 9.13	47.81 \pm 7.75*	40.46 \pm 7.04	30.22 \pm 4.21*
t		0.013	2.402	0.355	5.755	0.155	9.012
p		0.990	0.020	0.724	<0.001	0.877	<0.001

Note: Compared with before treatment in the same group, *p<0.05

TABLE 7: COMPARISON OF IMMUNE FUNCTION INDICES BEFORE AND AFTER TREATMENT IN THE TWO PATIENT GROUPS ($\bar{x}\pm s$, g/l)

Group	Number of cases	IgA		IgG		IgM	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation	30	2.02 \pm 0.44	2.11 \pm 0.36*	12.59 \pm 1.55	12.71 \pm 1.30*	1.74 \pm 0.34	1.82 \pm 0.51*
Control	30	2.03 \pm 0.48	2.05 \pm 0.41*	12.61 \pm 1.53	12.63 \pm 1.41*	1.75 \pm 0.33	1.79 \pm 0.48*
t		0.084	0.602	0.050	0.228	0.116	0.235
p		0.933	0.549	0.96	0.820	0.908	0.815

Note: Compared with before treatment in the same group, *p>0.05

TABLE 8: COMPARISON OF GASTROINTESTINAL HORMONE LEVELS BEFORE AND AFTER TREATMENT IN THE TWO PATIENT GROUPS ($\bar{x}\pm s$, ng/l)

Group	Number of cases	MTL		GAS	
		Before treatment	After treatment	Before treatment	After treatment
Observation	30	285.45 \pm 45.64	368.33 \pm 49.57*	77.48 \pm 10.14	98.02 \pm 13.82*
Control	30	284.97 \pm 44.74	323.34 \pm 50.72*	77.79 \pm 10.06	84.73 \pm 11.59*
t		0.041	3.475	0.119	4.036
p		0.967	0.001	0.906	<0.001

Note: Compared with before treatment in the same group, *p<0.05

The gallbladder wall affected by chronic cholecystitis undergoes various pathological changes with the progression of the disease, ultimately leading to pathological thickening of the gallbladder wall and adhesion to surrounding tissues under the influence of inflammatory factors^[13]. Chronic cholecystitis belongs to the category of gallbladder distension and hypochondriac pain in TCM. According to traditional Chinese medical theory, the liver and gallbladder are mutually interconnected organs, and they jointly regulate the qi-dispersion function, which is closely related to the regulation of the body's qi mechanism. If the liver and gallbladder fail to function properly, qi-dispersion becomes obstructed, qi mechanism is imbalanced, and bile excretion is impeded, leading to clinical manifestations such as significant discomfort in the hypochondriac region associated with chronic cholecystitis^[14]. Chinese medical experts throughout history have considered chronic cholecystitis to be a disease of both deficiency and excess, and the principle of treatment should focus on addressing both the root and the manifestations^[15]. Based on clinical observations, TCM theory believes that damp-heat is one of the most common and important pathogenic factors that induce cholecystitis. According to the pathogenic pathways, damp-heat is classified into two categories; exogenous pathogenic factors of the six exogenous evils and endogenous pathological changes of the Zang-Fu organs due to unregulated diet and psychological factors^[16,17].

Wen Dan Tang (WDT), derived from the medical classic *Ji Yan Fang* compiled by the renowned physician Yao Sengtan in the Northern and Southern Dynasties, has been found in clinical practice to have the functions of regulating qi, clearing heat, and resolving phlegm.

According to the principles of formula composition, WDT selects Chaihu (*Radix Bupleuri*) as the principal herb to regulate the liver and qi, and to facilitate the function of the liver and gallbladder. The herb Huangqi (*Astragalus membranaceus*), with its cold and bitter properties, enhances the heat-clearing and liver-soothing effects of Chaihu. Zhiqiao (*Fructus Aurantii*) promotes qi and relieves stagnation, Banxia (*Rhizoma Pinelliae*) dries dampness and resolves phlegm, and Chenpi (*Pericarpium Citri Reticulatae*) regulates qi and relieves distension. These three herbs, when combined with Chaihu, further enhance its qi-regulating effects. Chenpi and Zhiqiao also have the effect of relieving qi pain. Fuling (*Poria cocos*) dries dampness and resolves

phlegm while nourishing the spleen and stomach. Gancào (*Radix Glycyrrhizae*) and Baishao (*Radix Paeoniae alba*) have the effect of softening the liver and relieving pain. These herbs work synergistically to achieve the therapeutic effects of softening the liver, regulating qi, relieving spasms and pain, clearing heat, and resolving phlegm. The core herb combination in WDT is "Huangqi-Chaihu-Banxia." Modern pharmacological studies have shown that compounds such as quercetin^[18], baicalin, Beta (β)-glucosterol, kaempferol, and wogonin are important drug targets for the treatment of chronic cholecystitis. The progression of chronic cholecystitis is closely related to lipid metabolism. Based on existing research, quercetin can inhibit the differentiation and formation of preadipocytes and significantly inhibit the expression of inflammatory factors such as TNF- α in adipose tissue, thereby controlling the progression of chronic cholecystitis^[19]. Currently, Huangqi (*Astragalus membranaceus*) has become a research hotspot in clinical studies due to its unique pharmacological active ingredients baicalin and wogonin. Baicalin has been shown to effectively regulate cholesterol metabolism within the body by inhibiting the activity of liver X receptor α , ultimately reducing blood lipid levels and delaying the formation of gallbladder stones. Additionally, baicalin can assist in controlling pathological changes in the gallbladder wall induced by unhealthy dietary habits^[20]. Modern research has found that wogonin has good antioxidant effects. This compound inhibits intracellular reactive oxygen species, thereby affecting the Nuclear Factor-Kappa B (NF- κ B) signaling pathway in cells. Its unique pharmacological mechanism can effectively reduce the activity of inflammasomes and inhibit the inflammatory response of macrophages, inhibiting the expression levels of IL-8 and TNF- α in the body. Therefore, the results of this study showed that the levels of inflammatory factors in the observation group were lower than those in the control group during the same period^[21]. Kaempferol, a flavonoid compound, can inhibit cyclooxygenase and control the level of inflammation when local mucosal damage occurs in the gallbladder wall of patients with chronic cholecystitis^[22]. β -glucosterol can bind to cholesterol receptors and control cholesterol levels in the body, delaying the formation and occurrence of stones^[23]. Moreover, chronic cholecystitis often accompanies gastrointestinal discomforts such as abdominal distension and anorexia, significantly affecting patients' quality of life. In Wendan Tang

(a TCM formula), flavonoid compounds, the main active ingredient of *Fructus Aurantii*, have been found to regulate gastrointestinal motility in relevant studies. This not only improves patients' clinical gastrointestinal symptoms and quality of life, but also stimulates the secretion of cholecystokinin and MTL, thereby promoting gallbladder emptying^[24]. Based on the findings of this study, the levels of MTL and GAS in the observation group were higher than those in the control group, thanks to the regulation of gastrointestinal motility by the active ingredients in *Fructus Aurantii*, especially the stimulatory effect on MTL and GAS. Similarly, *Radix Paeoniae Alba* and *Radix Glycyrrhiza* are commonly used in TCM. Modern research has shown that the combination of *Radix Paeoniae alba* and *Radix Glycyrrhiza* exhibits a synergistic effect, increasing the contents of oxypaeoniflorin, albiflorin, and benzoylpaeoniflorin. These chemical components inhibit the expression of inflammatory factors IL-1 β , TNF- α , and PGE2 by acting on the IL-17, TNF, and NF- κ B signaling pathways, resulting in a good anti-inflammatory effect^[25]. Xiaoyan Lidan Pian (an anti-inflammatory and gallbladder-regulating pill) is recorded in the Chinese Pharmacopoeia^[26], and its main active ingredients include chlorogenic acid, rosmarinic acid, andrographolide, apigenin, and dehydrated andrographolide. It is clinically used for the treatment of acute and chronic cholecystitis and gallstones. The results of this study indicate that the comprehensive therapeutic effect of the observation group was better than that of the control group, suggesting that the combination of modified Wendan Tang and Xiaoyan Lidan Pian significantly improves clinical outcomes for patients.

In summary, the combination of modified Wendan Tang and Xiaoyan Lidan Pian is effective in suppressing the expression levels of inflammatory factors, improving clinical symptoms, reducing inflammation, and minimizing trauma to the patient's body in elderly patients with chronic cholecystitis. This treatment regimen is safe and effective, with few adverse reactions and no hepatorenal toxicity observed in clinical studies. However, the sample size of this study was relatively small, and long-term follow-up and observation of patients' clinical outcomes were not conducted. Therefore, future multicenter, large-scale, and long-term clinical studies are needed to further observe the clinical efficacy of modified Wendan Tang in elderly patients with chronic cholecystitis and improve the accuracy

of the research results.

Author's contributions:

Jing Han and Jingchao Chen have contributed same to this work and they both were considered as first authors.

Conflict of interests:

The authors declared no conflict of interests.

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