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Original Research Article

Therapeutic effect of He-Wei-Tong-Xie decoction on acute pancreatitis complicated with gastrointestinal dysfunction

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Abstract

Purpose: *To study the therapeutic effect of He-Wei-Tong-Xie (HWXT) decoction on acute pancreatitis (AP) complicated with gastrointestinal dysfunction.*
Methods: *AP patients (50) were recruited from the Teaching Hospital of Chengdu University of Traditional Chinese Medicine and randomly divided into treatment and control groups (25 per group). All patients were evaluated at baseline, and thereafter subjected to standard therapeutic protocols, including, fasting, gastrointestinal decompression, administration of somatostatin and omeprazole. The patients in the treatment group also received 100 mL of HWTX by nasal route with high enema (three times/day). Gastrointestinal function scores (stomach ache, abdominal distension, borborygmus and defecation), and hospitalization time were evaluated on days 3 and 7 of treatment.*
Results: *No significant baseline differences were observed between the treatment and control groups with respect to etiological agents and AP syndrome scores ($p > 0.05$). However, after 3 and 7 days of treatment, all AP syndromes in treatment group showed significant improvement compared with the control patients ($p < 0.01$). There were no significant differences in hospitalization time and rate of recovery between the treatment and control groups ($p < 0.01$).*
Conclusion: *HWTX treatment appears to be a safe and potentially useful approach for treating AP complicated with gastrointestinal dysfunction.*

Keywords: *He-Wei-Tong-Xie decoction, Acute pancreatitis, Gastrointestinal dysfunction, Somatostatin, Omeprazole*

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INTRODUCTION

Acute pancreatitis (AP), known as a common critical threatening disease in clinics, is a serious inflammatory disorder of the pancreas [1,2]. AP induces local and systemic complications, especially gastrointestinal dysfunction which could result in gut-derived infection, sepsis, multiple organ dysfunction syndromes (MODS), and death [2-4]. Although diagnostic technology for AP has improved appreciably over the years, effective treatment drugs with low side-effects are still lacking [5,6].

It is well known that traditional Chinese medicine (TCM) has been used to treat various diseases for thousands years in China, and the curative effects of most of these TCM formulas have been demonstrated in modern pharmacological studies [7-9]. In addition, increasing investigations have indicated that TCM formulas offer feasible approaches for treating AP due to their promising

effects on inflammatory and pain disorders, abdominal distension and constipation [8,10-12].

He-Wei-Tong-Xie (HWTX) decoction is an empirical TCM formula composed of *Codonopsis pilosula, Poriacocos, Atractylodes macrocephala, Citrus reticulata, Pinellia ternate, Rheum palmatum, Citrus aurantium, Magnolia officinalis, Euphorbia kansui, Glycyrrhiza uralensis* and Glauber salt (Table 1). It has been widely used in our hospital for treating acute pancreatitis complicated with gastrointestinal dysfunction. However, there have been no clinical or experimental studies on HWTX.

In the present study, we investigated the therapeutic effect of HWTX decoction on AP complicated with gastrointestinal dysfunction in patients from the Teaching Hospital of Chengdu University of Traditional Chinese Medicine.

EXPERIMENTAL

Subjects

The subjects were selected from patients admitted for treatments from June1, 2013 to December 30, 2014 in the Department of Emergency at The Affiliated Hospital of Chengdu University of Traditional Chinese Medicine (Chengdu, China). Male and female patients between the ages of 18 and 70 years were enrolled if they had definite diagnosis of AP. The diagnostic criteria were according to the Guidelines for the diagnosis and treatment of acute pancreatitis in China. These were (1) constant upper abdominal pain radiating to the back; (2) very high plasma levels of amylase and lipase (3 times the normal values) and (3) typical AP characteristic image changes by CT/MRI or abdomen ultrasound. A definite diagnosis was indicated by detection of any two of these criteria. All patients were required to read and sign informed consent forms voluntarily before enrollment. The study protocols were approved by the Ethics Committee of the affiliated hospital of Chengdu University of Traditional Chinese Medicine (no. 2013KL-035) (Chengdu, China).

Preparation of *He-Wei-Tong-Xie* decoction

HWTX is usually prepared by water decoction. Thus, the components of HWTX (Table 1) were decocted by auto drug decocting machine (North Pharmaceutical Equipment Manufacturing Co., Weifang, China) with 1500mL of water after soaking for 30 min. Extraction was done three times on the same sample. The extracts were pooled and filtered, and the clear supernatant was subsequently concentrated to 600 mL by using a rotary evaporator.

Study design

A total of 50 patients were divided randomly into treatment group and control group, each consisting of 25 patients. All patients were evaluated at baseline. Thereafter patients in both groups were treated with standard therapeutic protocols according to the Guidelines for the diagnosis and treatment of acute pancreatitis in China [13]. These included guardianship care, fasting, gastrointestinal decompression, and administration of somatostatin and omeprazole. Patients with biliary pancreatitis were given antibiotics and intravenous infusion. In addition to the standard treatments, the treatment group patients were administered 100 mL of HWTX by nasal feeding (three times/day), along with high enema, also given three times/day.

Efficacy assessment

Gastrointestinal function (stomachache scores, abdominal distension scores, borborygmus scores and defecation scores); hospitalization time, rate of disappearance of symptoms, and safety were evaluated at 3 and 7 days during treatment.

Table 1: Composition of HWTX

Plant	Family	Part of plant	Weight
Codonopsis pilosula	Campanulaceae	Root	25 g
Poriacocos	Polypores	Sclerotium	15 g
Atractylodes macrocephala	Asteraceae	Rhizoma	12 g
Citrus reticulate	Rutaceae	Pericarp	10 g
Pinellia ternate	Araceae	Tuber	8 g
Rheum palmatum	Polygonaceae	Root & Rhizoma	10 g
Citrus aurantium	Rutaceae	Fruit	10 g
Magnolia officinalis	Magnoliaceae	Cortex	10 g
Euphorbia kansui	Euphorbiaceae	Tuber	0.5 g
Glycyrrhiza uralensis	Leguminosae	Root	10 g
Glauber salt	-	-	10 g

The quantitative criteria for AP symptoms in our present investigation (Table 2) were drawn in line with previous reports [3,13,14]. In addition, gastrointestinal function recovery criteria were graded as: (1) clinical control: total scores decreasing ≥ 95 %; (2) markedly effective: total scores decreasing ≥ 70 %; (3) effective: total scores decreasing ≥ 30 %; (4) ineffective: total scores decreasing < 30 %; (5) or aggravated: total scores increasing > 0.

Safety evaluation

Adverse reactions were recorded during the investigation. Body temperature, heart rate, respiratory rate and blood pressure were monitored and routine hemogram, urinalysis, and liver and renal function tests were performed. The onset time, severity, frequency, duration, counter-measures and consequences of adverse reactions were recorded in detail.

Statistical analysis

Data are expressed as mean ± SD, and were analyzed using SPSS software (SPSS for windows 21.0, SPSS Inc, USA. Measurement data were analyzed by two-tailed t- test, while enumeration data were analyzed by Chi-square test. Grade comparison was by rank sum test. Differences were considered significant at $p < 0.05$.

RESULTS

Baseline demographics and disease characteristics

The baseline characteristics observed patients (age, breathing, body temperature and blood pressure) are shown in Table 3 while other baseline characteristics (white blood cell, WBC), neutrophil granulocyte, N), C reactive protein, CRP) and amylase are given in Table4. As can be seen from the Table, no statistically significant differences were observed between the treatment group and control group at baseline ($p > 0.05$).

AP scores

A similar result was obtained for AP scores (Table 5). Compared with patients in control group, no difference was seen in patients of treatment group in stomach ache, abdominal distension, borborygmus, and failure of stool and gas pass ($p > 0.05$).

Stomachache, abdominal distension, borborygmus and defecation scores

After 3 and 7 days of treatment, we compared stomach ache, abdominal distension, borborygmus and defecation scores between the two groups. As can be seen from Tables 6 - 8, patients in treatment group showed significant improvement in all the syndromes of AP compared with the control patients ($p < 0.01$).

Disappearance of AP symptoms, hospitalization time and adverse reactions after treatment

Results for comparison of rate of disappearance of AP symptoms, hospitalization time and adverse reactions after treatment are shown on Tables 9 - 12. No significant differences were observed between the treatment and control groups with respect to these parameters ($p > 0.05$).

Table 2: Quantitative criteria for symptoms of AP

Variable	0	2	4	6
Stomach	No	Tolerable, VAS:1-3	Occasional request for analgesia; VAS: 4-6	Need analgesia, VAS: 7-10
Abdominal distension	No	Tolerable, VAS was 1-3	Abdominal distension, VAS: 4-6	Abdominal distension, VAS: 7-10
Borborygmus	Normal (4-5 /min)	1-2/min	No	
Failure of stool and intestinal flatulence	No	Failure of stool, and defecation after enema.	Failure of stool, and intestinal flatulence	

VAS: Visual Analogue Scale/Score

Table 3: Baseline demographics and disease characteristics

Variable		Treatment (n=25)	Control (n=25)	*p* -value
Age				
	Mean	49.72 ± 13.67	45.32 ± 12.74	0.2440
	Min-Max	23.00 - 75.00	25.00 - 71.00	
	Med	47.00	43.00	
	Q1-Q3	40.00 - 59.50	35.50 - 54.50	
Breathing				
	Mean ±_SD	26.28 ± 2.85	25.16 ± 3.26	0.2023
	Min-Max	22.00 - 34.00	20.00 - 34.00	
	Med	26.00	26.00	
	Q1-Q3	24.00 - 28.00	22.00 - 26.50	
Body temperature				
	Mean ±_SD	37.24 ± 0.84	37.32 ± 1.01	0.7390
	Min-Max	36.00 - 38.30	36.00 - 39.20	
	Med	37.30	37.30	
	Q1-Q3	36.50 - 38.15	36.50 - 38.25	
Heart rate				
	Mean ±_SD	96.40 ± 15.93	96.60 ± 14.55	0.9632
	Min-Max	45.00 - 132.00	62.00 - 135.00	
	Med	98.00	98.00	
	Q1-Q3	89.00 - 102.00	88.50 - 102.50	
Systolic pressure				
	Mean ± SD	127.56 ± 15.56	123.24 ± 17.25	0.3572
	Min-Max	101.00 - 170.00	98.00 - 168.00	
	Med	123.00	122.00	
	Q1-Q3	119.50 - 136.00	109.50 - 137.00	
Diastolic pressure				
	Mean ± SD	76.76 ± 12.64	77.64 ± 10.64	0.7912
	Min-Max	48.00 - 111.00	60.00 - 107.00	
	Med	73.00	76.00	
	Q1-Q3	69.00 - 82.50	70.50 - 85.50	

Table 4: Baseline disease characteristics

	Treatment (n=25)	Control (n=25)	*p* value
White blood cell			
Normal	9 (36.00%)	8 (32.00%)	0.7653
Abnormal	16 (64.00%)	17 (68.00%)	
Neutrophils			
Normal	1 (4.00%)	3 (12.00%)	0.6092
Abnormal	24 (96.00%)	22 (88.00%)	
C reactive protein			
Normal	19 (76.00%)	14(56.00%)	0.1355
Abnormal	6 (24.00%)	11 (44.00%)	
Amylase			
Normal	2 (8.00%)	3 (12.00%)	1.0000
Abnormal	23 (92.00%)	22 (88.00%)	

Table 5: AP scores of patients before treatment

Variable	Score	Treatment (n=25)	Control (n=25)	*P*-value
Stomachache	4.00	10 (40 %)	10 (40 %)	1.0000
	6.00	15 (60 %)	15 (60 %)	
Abdominal distension	2.00	2 (8 %)	3 (12 %)	0.4189
	4.00	15 (60 %)	10 (40 %)	
	6.00	8 (32 %)	12 (48 %)	
Borborygmus	2.00	8 (32 %)	10 (40 %)	0.5597
	4.00	17 (68 %)	15 (60 %)	
Failure of stool and intestinal flatulence	0.00	0 (0 %)	2 (8 %)	0.9545
	2.00	10 (40 %)	7 (28 %)	
	4.00	15 (60 %)	16 (64 %)	

Table 6: Stomach ache scores of treatment and control groups

Variable	Score	Treatment (n=25)	Control (n=25)	Z	*P* value
Before Treatment	4.00	10(40.00%)	10(40.00%)	0.000	1.0000
	6.00	15(60.00%)	15 (60.00%)		
Three days' treatment	0	2(8 %)	0(0 %)	-3.024	0.0025
	2.00	11(44 %)	4(16 %)		
	4.00	11(44 %)	15(60 %)		
	6.00	1(4 %)	6(24 %)		
Seven days' treatment	0	4(16 %)	0(0 %)	-3.032	0.0024
	2.00	19(76 %)	15(60 %)		
	4.00	1(4 %)	6(24 %)		
	6.00	1(4 %)	4(16 %)		
Intra-group comparison	**Z**	-4.396	-3.640		
	***P* value**	0.000	0.000		

Table 7: Abdominal distension scores of treatment and control groups

Variable	Score	Treatment (n=25)	Control (n=25)	Z	*P*-value
Before treatment	2.00	2(8 %)	3(12 %)	-0.808	0.4189
	4.00	15(60 %)	10(40 %)		
	6.00	8(32 %)	12(48 %)		
Three days' treatment	2.00	19(76 %)	8(32 %)	-3.369	0.0011
	4.00	6(24 %)	13(52 %)		
	6.00	0(0 %)	4(16 %)		
Seven days' treatment	0	10(40 %)	2(8 %)	-2.678	0.0074
	2.00	11(44 %)	14(56 %)		
	4.00	4(16 %)	6(2 %)		
	6.00	0(0 %)	3(12 %)		
Intra-group comparison	**Z**	-4.396	-3.739		
	p **value**	0.000	0.000		

Table 8: Borborygmus scores of treatment and control groups

	Scores	Treatment (n=25)	Control (n=25)	Z	*P*-value
Before Treatment	2.00	8(32 %)	10(40 %)	-0.583	0.5597
	4.00	17(68 %)	15(60 %)		
Three days' treatment	0	6(24 %)	0(0 %)	-3.159	0.0016
	2.00	16(64 %)	14(56 %)		
	4.00	3(12 %)	11(44 %)		
Seven days' treatment	0	10(40 %)	5(20 %)	-2.367	0.0179
	2.00	15(60 %)	14(56 %)		
	4.00	0(0 %)	6(24 %)		
Intra-group comparison	**Z**	-4.072	-3.276		
	***P* value**	0.000	0.001		

Table 9: Defecation scores of treatment and control groups

Variable	Scores	Treatment (n=25)	Control (n=25)	Z	*P*-value
Before Treatment	0	0(0 %)	2(8 %)	-0.057	0.9545
	2.00	10(40 %)	7(28 %)		
	4.00	15(60 %)	16(64 %)		
Three days' treatment	0	6(24 %)	1(4 %)	-2.300	0.0215
	2.00	18(72 %)	20(80 %)		
	4.00	1(4 %)	4(16 %)		
Seven days' treatment	0	16(64 %)	13(52 %)	-0.902	0.3668
	2.00	8(32 %)	10(40 %)		
	4.00	1(4 %)	2(8 %)		
Intra-group comparison	**Z**	-4.388	-3.697		
	***P* value**	0.000	0.000		

Table 10: Rate of disappearance of AP symptoms

Variable	Result	Treatment (n=25)	Control (n=25)	χ^2	*P*-value
Stoma chache	Disappeared	4(16 %)	0(0 %)	4.348	0.1099
	Existed	21(84 %)	25(100 %)		
Abdominal distension	Disappeared	10(40 %)	2(8 %)	7.018	0.0181
	Existed	15(60 %)	23(92 %)		
Borborygmus	Disappeared	10(40 %)	5(20 %)	2.381	0.1228
	Existed	15(60 %)	20(80 %)		
Failure of stool and gas pass	Disappeared	16(64 %)	12(52 %)	0.689	0.4064
	Existed	9(36.00%)	11(47.83%)		

Table 11: Hospitalization time of treatment and control groups

Variable	Treatment (n=24)	Control (n=21)	*p* value
Full analysis set			
Mean_SD	12.46±5.85	18.10±4.96	0.0000
Min-Max	6.00 - 36.00	10.00 - 31.00	
Med	11.50	18.00	
Q1-Q3	9.00 - 13.75	15.50 - 20.00	
Per protocol set			
Mean_SD	12.46±5.85	18.10±4.96	0.0000
Min-Max	6.00 - 36.00	10.00 - 31.00	
Med	11.50	18.00	
Q1-Q3	9.00 - 13.75	15.50 - 20.00	

Table 12: Adverse reactions of treatment and control groups

Variable	Adverse reactions	Rate %	*P*-value
Treatment (n=25)	4	16.00	0.6671
Control (n=25)	2	8.00	

DISCUSSION

To the best of our knowledge, the present clinical report is the first experimental evidence regarding the therapeutic effects of HWTX decoction on AP complicated with gastrointestinal dysfunction. Interestingly and importantly, the results show that HWTX administration is beneficial in the treatment of AP with gastrointestinal dysfunction.

AP, a common acute abdominal disease, results from inflammatory reactions which damage the pancreas [3,15]. It causes acute stress, resulting in releases of various inflammatory cytokines and free radicals [3,16]. AP can easily lead to edema and erosion of digestive tract mucosa, resulting in the damage of mucosal barrier. This induces gut-derived infections due to translocation of gut bacterial endotoxin into blood [3,12]. Previous reports demonstrated that prognosis of AP patients can be greatly improved through recovery of gastrointestinal function and protection of gastrointestinal mucosal barrier. HWTX is derived from classical TCM formula of Large Chengqi Decoction and is composed of *C. pilosula, P. cocos, A. macrocephala, C. reticulata, P. ternate, R. palmatum, C. aurantium,* and *M. officinalis*. HWTX is an anti-bacterial agent which is also known to purge heat and flatulence from the bowels. Previous studies showed that the herbal components of HWTX possess significant beneficial effects against inflammatory reactions and gastrointestinal dysfunction [12,17,18]. In the present investigation, the results obtained indicate that HWTX in combination with standard AP treatment significantly improved AP syndromes when compared with control patients. The results also reveal that HWTX treatment is safe, with minimal side-effects.

Limitation of the study

In this work, the number of patients enrolled in the study is small, and therefore, a much higher number of patients would be required in future studies to validate the therapeutical effect of HWTX.

CONCLUSION

The findings of the present clinical study suggest that HWTX decoction is a safe and useful potential therapy for AP complicated with gastrointestinal dysfunction. However, further clinical studies are required confirm the findings obtained in this work.

DECLARATIONS

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Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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