ORIGINAL RESEARCH

Clinical Observation of Treatment Efficacy in Critical Paralytic Ileus Disease with Integrated Traditional Chinese and Western Medicine: A Randomized Controlled Trial

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ABSTRACT

Objective • The study aimed to evaluate the treatment efficacy of the combination of Da-Cheng-Qi Decoction (DCQD) injected into the jejunum and as an enema in patients with critical diseases with paralytic ileus.

Methods • In our double-blind randomized controlled study, 114 critically ill patients with paralytic ileus were divided into 2 groups. The control group received conventional medical treatment, and the DCQD group was treated with integrated traditional Chinese medicine (TCM) and Western medicine. The intra-abdominal pressure (IAP), recovery of gastrointestinal (GI) function, clinical efficacy and intensive care unit (ICU) stay in the 2 groups were recorded and compared.

Results • The IAP in the DCQD group was lower than in the control group ($P < .05$). The recovery of GI function and clinical efficacy rate in the DCQD group were significantly better than in the control group ($P < .05$, respectively).

Conclusion • DCQD may be an effective method for treating patients with critical diseases with paralytic ileus and is worthy of clinical application. (*Altern Ther Health Med.* 2022;28(3):30-33).

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INTRODUCTION

The gastrointestinal (GI) tract is the target organ of the body's critical stress response and one of the key links in the progression of critical diseases. GI dysfunction may cause intestinal bacteria and/or endotoxins to enter the bloodstream and cause enterogenic infection, mainly manifested as systemic inflammatory response syndrome, leading to multiple organ dysfunction syndrome, among which paralytic ileus is common in the early stage of critical diseases.[1]

GI motility drugs are mostly used clinically for paralytic ileus, but can cause problems such as delayed recovery of intestinal function and severe adverse drug reactions,[2] which are not conducive to a good prognosis in patients with critical diseases. Therefore, the effective treatment of GI dysfunction with minor adverse events in critical diseases has become the focus of clinical research. Recently, it has been found that Da-Cheng-Qi Decoction (DCQD), a classic Chinese medicine prescription, has a good effect in the treatment of both patients with paralytic ileus and severe acute pancreatitis in rats.[3-5]

In Traditional Chinese Medicine (TCM), critically ill patients have an obstruction of Qi and Xue, lifting abnormal, which leads to reduced bowel movements, abdominal pain, bloating and dry stools.[6] DCQD is a famous classic prescription in the *Shang Han Lun*, a classic work of TCM written approximately 1800 years ago.

To further investigate and confirm the effect of DCQD on paralytic ileus in critically ill patients, we conducted this prospective randomized controlled trial.

MATERIALS AND METHODS

Inclusion and Exclusion Criteria

From January 2016 to September 2019, a total of 114 consecutive critically patients with paralytic ileus admitted to the intensive care unit were prospectively enrolled in the study.

Inclusion criteria. (1) Patients who met the diagnostic criteria for severe GI dysfunction in critical care medicine;[7] (2) patients with acute gastrointestinal injury (AGI) grade II and above;[8] (3) patients without severe metabolic diseases.

Exclusion criteria. Patients with GI bleeding or perforation, coagulopathy, heart failure, severe liver or kidney

dysfunction; (2) patients who were post-GI surgery or had colorectal diseases and could not tolerate enemas.

This research protocol conforms to the requirements of the World Medical Association's Declaration of Helsinki. The study was approved by the Ethics Committee of Wuhan First Hospital (ID: wy022). All patients signed an informed consent form.

Intervention

All enrolled patients were assigned to one of two groups: the control group or the DCQD group via the random number table method, with 57 patients in each group. The medical staff tasked to perform patient enrolment were blinded to this study.

Control group. The control group received conventional medical treatment, including fasting; GI decompression; maintenance of water, electrolyte and acid-base balance; and were provided with parenteral nutritional support as necessary. In addition, the control group was given 300 ml of normal saline injected into the jejunum twice a day, and the remaining 100 ml was used for an enema.

DCQD group. The DCQD group was treated with integrated TCM and Western medicine; that is, conventional medical treatment, including intra-jejunal perfusion and enema of the DCQD were performed. In addition, the DCQD group received prescriptions including 10 g each of rhubarb, mirabilite, magnolia officinalis, citrus aurantium, white peony root, bupleurum, scrophulariaceae, scutellaria, salvia and gardenia. Except for rhubarb and mirabilite, the herbs were decocted twice. Rhubarb was soaked separately for 30 minutes, added 5 minutes before the first decoction was completed and boiled with the other herbs during the second decoction. Mirabilite powder was used and added to the medicine bowl after decocting the medicine. Water was added to decoct the herbs to 400 mL, of which 300 mL was injected through a nasojejunal tube and the other 100 mL was used for an enema. Meanwhile, 300 g of mirabilite in a cloth bag was applied externally to the abdomen, which was changed every 12 hours for 7 days.

Observational index

Intra-Abdominal Pressure (IAP). Cystometry was used to dynamically monitor the daily IAP in the 2 groups before treatment and 7 days after treatment. To measure the IAP, the patient took a supine position and the medical staff performed a catheterization on each patient to empty their bladder. The piezometer tube was connected and 50 mL of normal saline was injected into the bladder through a piezometer tube. The piezometer tube was placed perpendicular to the bed surface, the pubic symphysis was taken as the zero point and the height of the water column was the IAP value.

GI Recovery Index and Length of ICU Stay. The GI recovery index in the 2 groups was observed, including the time of GI defecation, time of abdominal pain and abdominal distension relief and fasting time. The GI function recovery index was calculated from the day on which the diagnosis of paralytic ileus was made, using "day" as the unit of calculation.

Intestinal Permeability

Urinary lactofructose/mannitol ratio was measured on the first day after admission and on the fifth and tenth day after treatment. All urine within 4 hours after oral administration of 10 mL of the test solution (10 g lactulose and 5 g mannitol) was collected. The lactulose and mannitol values were tested with high pressure liquid chromatograph, and the ratio of lactulose /mannitol was calculated.

Clinical Efficacy

Efficacy evaluation criteria are as follows:[9]

(1) **Recovery**. The patient's GI symptoms have basically disappeared; a plain film of the abdomen shows that the obstruction is gone and bowel movement is restored. Patients may follow semi-liquid diets.
(2) **Significantly effective**. The patient's GI symptoms are significantly improved, abdominal plain film shows that the obstruction has been significantly relieved, bowel movement has recovered, and the patient can consume a semi-liquid diet.
(3) **Effective**. The patient's GI symptoms have been relieved, and abdominal plain film shows some improvement in the obstruction. After enema treatment, the patient can defecate normally but cannot consume a semi-liquid diet.
(4) **Invalid**. The ileus symptoms have not improved significantly and even worsened.

The total effective rate was the sum of recovery, the significantly effective, effective rate. In addition, any diarrhea was recorded.

Statistical Analysis

Measurement data are expressed as mean and standard deviation (SD), and t-test was used for the comparison between groups. Counting data are analyzed using the χ^2 test. The level of statistical significance for all was defined as a probability value of less than 0.05 ($P < .05$). All statistical analyses were performed using IBM® SPSS Statistics v19.8 software and based on intent-to-treat.

RESULTS

A total of 114 patients with various critical diseases were enrolled in and completed the study. The control group contained 32 men, 25 women, age range 25 to 76 years, mean age 52.7 ± 12.6 years and the DCQD group comprised 34 men, 23 women, age range 26 to 75 years, mean age 53.1 ± 13.2 years. The differences in gender; age; body mass index (BMI); primary illness; Acute Physiology, Age, Chronic Health Evaluation II (APACHE II) score and disease course in the 2 groups were not statistically significant ($P > .05$), as shown in Table 1. In addition, a total of 17 patients had diarrhea; 10 in the DCQD group and 7 in the control group. All patients received routine symptomatic treatment.

Table 1. Baseline Demographics (x ± s)

	Control Group (n = 57)	DCQD Group (n = 57)	*P* value
Gender (male/female)	32/25	34/23	
Age	52.7 ± 12.6	53.1 ± 13.2	.102
BMI (kg/m^2)	17.2 ± 2.3	17.5 ± 2.3	.106
Primary illness			
Severe pneumonia	18	19	
Severe pancreatitis	52	11	
Sepsis	17	16	
Myocardial infarction	10	11	
Course of disease (d)	2.5 ± 1.4	2.6 ± 1.5	.101
APACHE II	15.4 ± 4.2	15.5 ± 4.4	.097

Abbreviations: DCQD, Da-Cheng-Qi Decoction; BMI, body mass index; APACHE II, Acute Physiology, Age, Chronic Health Evaluation II.

Table 2. Comparison of IAP Value in the Two Groups (mmHg; x ± s)

Time	Control Group (n = 57)	DCQD Group (n = 57)	*P* value
Prior treatment	14.61 ± 2.63	14.97 ± 2.31	.082
1st day after treatment	13.34 ± 2.51	13.46 ± 2.46	.087
2nd day after treatment	12.29 ± 2.85	11.79 ± 2.14	.073
3rd day after treatment	11.49 ± 2.49	8.15 ± 1.81[a]	.042
4th day after treatment	10.57 ± 1.78	7.75 ± 1.46[a]	.041
5th day after treatment	9.96 ± 1.35	6.26 ± 1.22[a]	.042
6th day after treatment	8.89 ± 1.18	6.22 ± 1.14[a]	.045
7th day after treatment	7.81 ± 1.22	6.11 ± 1.07[a]	.045

[a]$P < .05$, DCQD group vs Control group

Abbreviations: DCQD, Da-Cheng-Qi Decoction; IAP, intra-abdominal pressure.

Table 3. Comparison of Gastrointestinal Function Recovery Indices and Length of ICU Stay in the Two Groups (d; x ± s).

Time	Control Group (n = 57)	DCQD Group (n = 57)	*P* value
Time of gastrointestinal exhaust and defecation	2.93 ± 0.86	1.82 ± 0.64[a]	.045
Time of abdominal pain and relief of abdominal distension	5.27 ± 1.35	3.21 ± 0.86[a]	.043
Time of borborygmus	5.68 ± 1.53	3.74 ± 1.14[a]	.044
Fasting time	6.24 ± 1.56	5.32 ± 1.36[a]	.044
Length of ICU stay	9.56 ± 1.74	8.56 ± 1.51[a]	.045

[a]$P < .05$, DCQD group vs Control group

Abbreviations: ICU, intensive care unit; DCQD, Da-Cheng-Qi Decoction.

Table 4. Comparison of the of Lactulose/Mannitol Ratio in the Two Groups

Time	Control group (n = 57)	DCQD group (n = 57)	*P* value
1st day after admission	0.097 ± 0.007	0.098 ± 0.007	.083
5th day after treatment	0.085 ± 0.005	0.066 ± 0.004[a]	.042
10th day after treatment	0.049 ± 0.003	0.025 ± 0.002[a]	.040

[a]$P < .05$, DCQD group vs Control group

Abbreviation: DCQD, Da-Cheng-Qi Decoction.

Table 5. Comparison of Curative Effect in the Two Groups (n, %)

Curative effect	Control Group (n=57)	DCQD Group (n=57)	χ^2	*P* value
Recovery	18 (31.6)	26 (45.6)	75.32	.042
Significant effective	16 (28.1)	21 (36.8)		
Effective	15 (26.3)	8 (14.0)		
Invalid	8 (14.0)	2 (3.5)		
Total effective rate	49 (86.0)	55 (96.5)		

Abbreviation: DCQD, Da-Cheng-Qi Decoction.

Comparison of IAP

After treatment, IAP values in both groups showed a trend toward gradually decreasing. From the third to the seventh day after treatment, IAP values in the DCQD group were significantly lower than in the control group, and the differences between the 2 groups were statistically significant ($P < .05$). (See Table 2.)

Comparison of GI Recovery Index and Length of ICU Stay

The time of GI defecation, abdominal pain and abdominal distension relief, fasting time and length of intensive care unit (ICU) stay in the DCQD group were significantly shorter than in the control group ($P < .05$, respectively; see Table 3).

Comparison of the Lactulose/Mannitol Ratio

Urinary lactulose/mannitol is often used to assess intestinal mucosal permeability. The higher the ratio of urinary lactulose/mannitol, the higher the permeability of the intestinal mucosa and the higher the degree of damage to the intestinal mucosa.

There was no significant difference in the lactulose/mannitol ratio between the 2 groups at admission ($P > .05$). The ratios decreased in both groups on the fifth and tenth day after treatment, and the difference was significant compared with the first day of admission ($P < .05$, respectively). Comparison between groups showed that the ratio of lactulose/mannitol in the DCQD group was lower than in the control group on the fifth and tenth day after treatment, with statistical significance ($P < .05$, respectively; shown in Table 4).

Comparison of Curative Effect

In the control group, there were 18 recovery patients (31.6%), 16 significant effective (28.1%), 15 effective (26.3%) and 8 invalid (14.0%); total effective rate was 86%. In the DCQD group, there were 26 recovery patients (45.6%), 21 significant effective (36.8%), 8 effective (14.0%) and 2 invalid (3.5%); total effective rate was 96.5%. The curative effect of integrated TCM and Western medicine is more obvious and was of statistical significance ($P < .05$) (see Table 5).

DISCUSSION

This study found that the traditional Chinese herbal medicine, DCQD, has a good therapeutic effect in paralytic ileus caused by severe diseases, can effectively relieve intestinal mucosal damage, promotes recovery of intestinal function and can shorten the length of ICU hospitalization.

Research has examined the potential use of DCQD enema in the treatment of paralytic ileus. A previous study confirmed that DCQD has the following pharmacological effects: (1) excites the intestines and strengthens GI peristalsis; (2) improves GI local blood flow, increases arterial oxygen partial pressure and reduces GI stress; promotes the release of motilin, vasoactive intestinal peptide and substance P and promotes the recovery of GI function; (3) has antibacterial and anti-inflammatory effects, reduces capillary permeability, reduces inflammatory exudation, inhibits intestinal flora migration and/or endotoxins from entering the blood and prevents enterogenous infection. However, these hypotheses remain to be proven in future studies.

Under normal circumstances, the human intestinal mucosa can effectively prevent toxins, bacteria and other harmful substances from entering the body. However, in the case of surgery, infection, inflammation and intestinal diseases, intestinal mucosal barrier function can be damaged, manifested as mesenteric vasospasm, intestinal mucosal atrophy and damage. The increase in intestinal permeability has already occurred before the obvious changes in intestinal mucosal morphology are seen. Therefore, an increase in intestinal mucosal permeability can reflect early intestinal mucosal barrier damage.

A 2019 study found that urinary excretion of 2 orally-administered non-metabolizable sugars, lactulose and mannitol, was a valuable marker for evaluating intestinal permeability.[11] In our study, there was no significant difference between the 2 groups in the lactulose/mannitol ratio on the first day after admission. On the fifth and tenth days after treatment, the lactulose/mannitol ratio increased in both groups, indicating that intestinal barrier function was impaired and mucosal permeability increased. The lactulose/mannitol ratio in patients receiving integrated TCM and Western medicine treatment was significantly lower than in the control group, indicating that this treatment can promote recovery of GI mucosal barrier function damage caused by stress in critically ill patients, thereby reducing intestinal bacterial translocation and the chance for intestinal infection.

The IAP measurement is becoming more and more important in critically ill patients with acute abdominal pain, and vesical IAP measurement is considered the gold standard of IAP measurement.[12] The results of this study showed that although the IAP in both groups showed a downward trend after treatment, the IAP in the DCQD group was significantly lower than in the control group. GI function recovery in the DCQD group was significantly better than in the control group from the third day to the seventh day after treatment. This result also verified the effect of DCQD on organ function recovery.

Study Limitations

This study has certain limitations. First, it is a single-center trial, making selection bias inevitable. Second, this study was mainly concerned with the observation of clinical phenomena, and no mechanism was explored.

CONCLUSION

In the treatment of patients with critical diseases with paralytic ileus, compared with pure Western medicine treatment, integrated TCM and Western medicine can effectively improve the clinical cure rate and shorten the time needed for clinical symptom relief, and is worthy of clinical application.

AUTHOR CONTRIBUTIONS

Hongjun Ye, BM andGuangwu Jing, MM contributed equally to this paper.

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