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RAPID COMMUNICATION

Treatment of abdominal compartment syndrome in severe acute pancreatitis patients with traditional Chinese medicine

Min-Jie Zhang, Guo-Lei Zhang, Wen-Bin Yuan, Jun Ni, Li-Feng Huang

Min-Jie Zhang, Guo-Lei Zhang, Wen-Bin Yuan, Jun Ni, Department of General surgery, Affiliated Central Hospital of Huzhou Normal College, Huzhou 313000, Zhejiang Province, China
Li-Feng Huang, Research Center of Biomedicine and Health, Hangzhou Normal University, Hangzhou 310000, Zhejiang Province, China
Author contributions: Zhang MJ and Zhang GL contributed equally to this work; Zhang MJ, Zhang GL, Yuan WB, and Ni J designed the research; Zhang MJ, Yuan WB, and Ni J performed the research; Huang LF provided the new reagents/analytic tools; Zhang MJ, Yuan WB, and Ni J analyzed the data; Zhang MJ, Yuan WB, and Huang LF wrote the paper.
Correspondence to: Min-Jie Zhang, Department of General surgery, Affiliated Central Hospital of Huzhou Normal College, Huzhou 313000, Zhejiang Province, China. zmjys@yahoo.com.cn
Telephone: +86-572-2369815 Fax: +86-572-2369815
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Abstract

AIM: To investigate the therapeutic effect of traditional Chinese traditional medicines *Da Cheng Qi* Decoction (Timely-Purging and Yin-Preserving Decoction) and Glauber's salt combined with conservative measures on abdominal compartment syndrome (ACS) in severe acute pancreatitis (SAP) patients.

METHODS: Eighty consecutive SAP patients, admitted for routine non-operative conservative treatment, were randomly divided into study group and control group (40 patients in each group). Patients in the study group received *Da Cheng Qi* Decoction enema for 2 h and external use of Glauber's salt, once a day for 7 d. Patients in the control group received normal saline (NS) enema. Routine non-operative conservative treatments included non-per os nutrition (NPON), gastrointestinal decompression, life support, total parenteral nutrition (TPN), continuous peripancreatic vascular pharmaceutical infusion and drug therapy. Intra-cystic pressure (ICP) of the two groups was measured during treatment. The effectiveness and outcomes of treatment were observed and APACHE Ⅱ scores were applied in analysis.

RESULTS: On days 4 and 5 of treatment, the ICP was lower in the study group than in the control group ($P < 0.05$). On days 3-5 of treatment, acute physiology and chronic health evaluation Ⅱ (APACHE Ⅱ) scores for the study and control groups were significantly different ($P < 0.05$). Both the effectiveness and outcome of the treatment with *Da Cheng Qi* Decoction on abdominalgia, burbulence relief time, ascites quantity, cyst formation rate and hospitalization time were quite different between the two groups ($P < 0.05$). The mortality rate for the two groups had no significant difference.

CONCLUSION: *Da Cheng Qi* Decoction enema and external use of Glauber's salt combined with routine non-operative conservative treatment can decrease the intra-abdominal pressure (IAP) of SAP patients and have preventive and therapeutic effects on abdominal compartment syndrome of SAP.

Key words: *Da Cheng Qi* Decoction; Glauber's salt; Traditional Chinese medicine; Severe acute pancreatitis; Abdominal compartment syndrome

Peer reviewer: Dr. Yukihiro Shimizu, Kyoto Katsura Hospital, 17 Yamada-Hirao, Nishikyo, Kyoto 615-8256, Japan

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INTRODUCTION

Severe acute pancreatitis (SAP) is a serious surgical disease with a mortality of 25%-40%[1,2]. Patients with SAP tend to have elevated intra-abdominal pressure (IAP), which eventually leads to intra-abdominal hypertension (IAH). IAH causes organ dysfunctions such as respiratory, circulatory and renal failure, known as abdominal compartment syndrome (ACS)[3,4]. About 11% of SAP patients suffer from complications of ACS. SAP patients complicated by ACS, a special type of pancreatitis, tend to have a mortality of 66.7%[5]. There are certain guidelines for treatment of SAP, but no standard treatment for ACS

in SAP patients is available at present[2]. In our previous study, *Da Cheng Qi* Decoction showed beneficial effects on acute pancreatitis (AP) with no adverse effects[6]. In the present study, we used *Da Cheng Qi* Decoction and Glauber's salt combined with routine non-operative conservative treatments, including non-per os nutrition (NPON), gastrointestinal decompression, life support, total parenteral nutrition (TPN), continuous peripancreatic vascular pharmaceutical infusion and drug therapy in the treatment of ACS in SAP patients. Through comparison with the control group, we demonstrated whether the TCM-wm therapy is effective for treatment of ACS in SAP patients.

MATERIALS AND METHODS

Patients

A total of 80 consecutive SAP patients were treated in the Surgery Department of Affiliated Central Hospital of Huzhou Normal College. The age of the patients ranged 27-76 years (mean 54.4 years, median 47 years). There were 38 males (47.5%) and 42 females (52.5%), the male to female ratio was 0.905:1. When they were hospitalized, the severity of SAP was evaluated according to the serum level of amylase, CT serious index (CTSI)[7], acute physiology and chronic health evaluation Ⅱ (APACHE Ⅱ) score[8], and the diagnostic criteria and severity grade for AP proposed by the Japanese Ministry of Health, Labor, and Welfare (JMHLW)[9]. The diagnosis of ACS was made as previously described[10]. Demographic data, serum level of amylase, CTSI, APACHE Ⅱ scores, ACS rate and severity grade ratio were not statistically different between the study and control groups (Table 1).

Table 1 Demographic data, serum level of amylase, CTSI score, APACHE Ⅱ score, ICP data and severity grade ratio of the two groups when hospitalized (mean ± SD)

	Study group (n = 40)	Control group (n = 40)
Age (yr)	54.2 ± 7.4	54.6 ± 8.1
Sex (male/female)	20/20	18/22
serum levels of amylase (U/L)	328.23 ± 13.89	354.51 ± 14.22
ICP (cmH_2O)	19.5 ± 3.4	18.7 ± 3.6
CTSI score	7.85 ± 1.1	7.90 ± 1.4
APACHE Ⅱ score	17.51 ± 4.51	18.2 ± 3.87
ACS rate (%)	17.5	20.0
Severity grade (Ⅱ/Ⅲ)	22/8	23/7

Methods

Eighty patients of SAP admitted for routine non-operative conservative treatment were randomly divided into study group and control group (40 patients in each group). Patients in the study group) received *Da Cheng Qi* Decoction enema (one dosage, 100 mL) for 2 h and external use of Glauber's salt (100 g) once a day for 7 d. Patients in the control group received 100 mL normal saline (NS) enema. One dosage of *Da Cheng Qi* Decoction consists of 10 g *Rheum officinale Baill*, 10 g *Sodium sulfate*, 10 g *Magnolia obavata*, 10 g *Fructus aurantii*, 10 g *Radix paeoniae rubra*, and 10 g *Raphanus sativus*. *Routine non-operative conservative* treatment modalities included NPON, gastrointestinal decompression, life support, TPN, continuous peripancreatic vascular pharmaceutical infusion[11,12] and drug therapy. Intracystic pressure (ICP) in the two groups could reflect the IAP conditions at admission and on days 1-7 of treatment. ICP data were defined as previously described[13]. Effectiveness of the treatment on abdominalgia, burbulence relief time, ascites quantity, cyst formation, mortality rate and hospitalization time were observed. The ascites quantity in patients was defined by B-ultrasound test on day 7 of treatment. APACHE Ⅱ scores, defined using Microsoft APACHE Ⅱ graded compute program version 5.1, were applied for analysis.

Statistical analysis

All data were prepared and compiled using the SPSS computer program (version 11.0 for windows). The data were expressed as mean ± SD. Kolmogorov-smirnov test was used for the pattern of data distribution. Student's unpaired t-test was used to compare data between the two groups when they were normally distributed. The Mann-Whitney U test was used when the data were not normally distributed. Chi square test and Fisher's exact test were used for quantitative data analysis. Step-wise regression analysis was used for multivariate analysis to determine any confounding factors. $P < 0.05$ was considered statistically significant.

RESULTS

ICP and APACHE Ⅱ scores

On days 4 and 5 of treatment, the ICP data obtained from the study group were lower than those obtained from the control group ($P < 0.05$). On days 3-5 of treatment, the APACHE Ⅱ scores of the study group and control group were significantly different ($P < 0.05$, Table 2). As shown in Table 2, the ICP data were significantly decreased from the 4th treatment day in the study group ($P < 0.05$), while significantly decreased from the 6th treatment day in the control group ($P < 0.05$). The cumulative scores of APACHE Ⅱ were significantly decreased from the 3rd treatment day in the study group ($P < 0.05$), while significantly decreased from the 6th treatment day in the control group ($P < 0.05$).

Effectiveness of treatment

As shown in Table 3, the relief time of abdominalgia and burbulence was shorter in the study group than in the control group ($P < 0.05$). The amount of ascites on day 7 of treatment was less in the study group than in the control group ($P < 0.05$).

Outcome of treatment

As shown in Table 4, the mortality rate was lower for the study group than for the control group, and there was no significant difference between the two groups. The cyst formation rate was significantly lower for the

Table 2 ICP and APACHE Ⅱ score of the two groups (n = 40, mean ± SD)

	ICP			APACHE Ⅱ scores		
	Study group	Control group	*P*	Study group	Control group	*P*
HPd	19.5 ± 3.4	18.7 ± 3.6		17.51 ± 4.51	18.2 ± 3.87	
Day 1	16.5 ± 3.2	17.4 ± 3.8		16.44 ± 3.54	17.85 ± 4.12	
Day 2	15.8 ± 2.5	16.2 ± 1.9		14.21 ± 4.23	16.55 ± 3.98	
Day 3	15.6 ± 2.7	15.9 ± 3.1		9.66 ± 1.88[c]	13.46 ± 1.93	< 0.05
Day 4	8.2 ± 1.5[a]	15.2 ± 3.7	< 0.05	7.41 ± 1.72[c]	12.37 ± 2.21	< 0.05
Day 5	8.7 ± 3.2[a]	14.7 ± 2.9	< 0.05	4.63 ± 1.46[c]	10.78 ± 2.01	< 0.05
Day 6	7.9 ± 3.9[a]	7.5 ± 3.5[a]		4.33 ± 2.01[c]	5.23 ± 2.67[c]	
Day 7	7.4 ± 2.8[a]	8.1 ± 2.7[a]		3.78 ± 1.53[c]	4.21 ± 1.62[c]	

[a]P < 0.05 *vs* ICP of HPd; [c]P < 0.05 *vs* APACHE Ⅱ scores of HPd. HPd: Hospitalization day.

Table 3 Relief time of abdominalgia and burbulence, ascites quantity on day 7 of treatment in the two groups (mean ± SD)

	Study group (n = 40)	Control group (n = 40)	*P*-value
Relief time of abdominalgia (d)	4.27 ± 0.87[a]	10.85 ± 1.21	0.035
Relief time of burbulence (d)	6.94 ± 1.22[a]	13.27 ± 3.67	0.021
Ascites quantity (mL)	457.25 ± 34.21[a]	927.84 ± 27.45	0.038

[a]P < 0.05 *vs* control group.

study group than for the control group (P < 0.05). The hospitalization time of the study group was significantly shorter than that of the control group (P < 0.05).

DISCUSSION

SAP is a serious pathological condition and SAP patients tend to suffer from ACS[14,15]. It was reported that SAP can result in systemic inflammatory response syndrome (SIRS) trigged by local inflammation in the panceas[16]. The fundamental pathophysiology of SIRS is hypercytokinemia, a pathological condition in which inflammatory cytokines are excessively released from immunocompetent cells[17]. During SIRS, activated inflammatory mediators result in the development of systemic capillary leakage syndrome (SCLS)[18]. In SCLS, vascular permeability is increased by the pathologic effects of humoral mediators, leading to interstitial edema and reduction of circulating blood volume[19]. Progressive edema of peritoneum and gut contents could rapidly increase IAP. Moreover, massive pancreatic liquid collection in the abdominal and retroperitoneal cavity and a large amount of pancreatic necrotic tissue combined with infection would lead to the formation of abscess, causing intestinal obstruction and erosion of the surrounding organs, which further result in perforation and massive bleeding and recurrence of SIRS and SCLS. Edema caused by the septic retroperitoneal necrosis pushes the peritoneum, thus rapidly increasing IAP[20]. Furthermore, for the treatment of SAP, early resuscitation with a large volume of fluid is essential to maintain organ perfusion. However, aggressive fluid resuscitation may aggravate intestinal edema, further increasing IAP[21], indicating that SAP can induce retroperitoneal edema or abscess, fluid collection in the abdominal and retroperitoneal cavity, intestinal edema, and that aggressive fluid resuscitation could increase IAP and abrupt elevation of IAP eventually causes IAH. IAH causes organ dysfunctions such as respiratory, circulatory and renal failure, known as ACS[22]. Since SAP patients with complication of ACS have a very high mortality, it is very important to find a right way to prevent and treat ACS in SAP patients.

Table 4 Mortality rate, cyst formation rate and hospitalization time of the two groups (mean ± SD)

	Study group (n = 40)	Control group (n = 40)	*P*-value
Mortality rate (%)	7.5 (3/40)	20.0 (8/40)	0.194
Cyst formation rate (%)	10.0 (4/40)[a]	32.5 (13/40)	0.029
Hospitalization time (d)	16.59 ± 3.89[a]	29.58 ± 4.52	0.037

[a]P < 0.05 *vs* control group.

Da Cheng Qi Decoction is a traditional Chinese medicine documented in Shang Han Lun (Treatise on Febrile Diseases). Its major components include Rheum officinale Baill, sodium sulfate, Magnolia obovata, Fructus aurantii, Radix paeoniae rubra, and *Raphanus sativus*. Modern clinical and experimental researches have focused on the effect of such components[23-25]. Glauber's salt, a sodium sulfate dehydrate (Na_2SO_4), is widely used as an anti-tissue edema agent in modern medical treatment[26,27]. Non-operative conservative treatment has been widely accepted for AP[28,29]. Especially, in our previous studies[11,12,30], continuous peripancreatic vascular pharmaceutical infusion could efficiently remove various humoral mediators and inflammatory cytokines from circulating blood, and decrease the mortality of SAP patients. In the present study, we used *Da Cheng Qi* Decoction and Glauber's salt combined with routine non-operative conservative treatments including continuous peripancreatic vascular pharmaceutical infusion for treatment of ACS in SAP patients.

In this study, the ICP data were lower in the study group than in the control group on days 4 and 5 of treatment (P < 0.05). The APACHE Ⅱ scores in study group were significantly less in the study group than in the control group on days 3-5 of treatment (P < 0.05). The ICP data were significantly decreased from the 4th treatment day in the study group (P < 0.05) while significantly decreased from the 6th treatment day in the control group (P < 0.05). The cumulative scores of APACHE Ⅱ were significantly decreased from the 3rd treatment day in the study group (P < 0.05) while significantly decreased from the 6 treatment day in the control group (P < 0.05). The relief time of abdominalgia and burbulence was shorter in the study group than in the control group (P < 0.05). The amount of ascites on day 7 of treatment was less in the study group than in the control group (P < 0.05). The cyst formation rate was significantly lower for the study group than for the

control group ($P < 0.05$). The hospitalization time was significantly shorter in the study group than in the control group ($P < 0.05$). These results suggest that *Da Cheng Qi* Decoction and Glauber's salt combined with non-operative conservative treatments including continuous peripancreatic vascular pharmaceutical infusion can treat IAH by decreasing IAP, relaxing symptoms of ACS, slowing down the pathological condition exacerbation, and accelerating the recovery of illness.

In summary, *Da Cheng Qi* Decoction and Glauber's salt combined with non-operative conservative treatments including continuous peripancreatic vascular pharmaceutical infusion (TCM-wm therapy) can prevent and treat ACS in SAP patients.

COMMENTS

Background

Severe acute pancreatitis (SAP) is a familiar surgical disease and about 11% of SAP patients suffer from abdominal compartment syndrome (ACS). SAP patients complicated by ACS tend to have a mortality of 66.7%. There are certain guidelines for treatment of SAP. However, no standard treatment for ACS in SAP patients is available at present.

Research frontiers

Da Cheng Qi Decoction is a traditional Chinese medicine documented in Shang Han Lun (Treatise on Febrile Diseases). Modern clinical and experimental research results have proved its effect. Glauber's salt is widely used as an anti-tissue edema agent in modern medical treatment. *Da Cheng Qi Decoction* or Glauber's salt has beneficial effects on SAP with no adverse effects. Non-operative conservative treatment, especially continuous peripancreatic vascular pharmaceutical infusion for SAP could efficiently remove various humoral mediators and inflammatory cytokines from circulating blood, and decrease the mortality of SAP patients.

Innovations and breakthroughs

In this study, *Da Cheng Qi* Decoction and Glauber's salt combined with routine non-operative conservative treatments, including continuous peripancreatic vascular pharmaceutical infusion were used in the treatment of ACS in SAP patients. Whether the TCM-wm therapy is effective for ACS in SAP patients was also studied. The results suggest that *Da Cheng Qi* Decoction and Glauber's salt can treat IAH by decreasing IAP, relaxing symptoms of ACS, slowing down the pathological condition exacerbation and accelerating the recovery of illness.

Applications

The study results provide an important new clue to the treatment of ACS in SAP patients.

Terminology

SAP is a serious type of acute pancreatitis (AP) complicated by pancreas necrosis and toxic shock. ACS is a syndrome due to factors that cause abrupt elevation of intra-abdominal pressure (IAP), leading to organ dysfunctions such as respiratory, circulatory and renal failure. *Da Cheng Qi* Decoction is a traditional Chinese medicine. Its major components include Rheum officinale Baill, sodium sulfate, Magnolia obovata, Fructus aurantii, Radix paeoniae rubra, and Raphanus sativus. Glauber's salt is a sodium sulfate dehydrate (Na_2SO_4). Acute physiology and chronic health evaluation Ⅱ (APACHE Ⅱ) is a disease classification system, which is used to evaluate the severity of disease. Intracystic pressure (ICP) is the pressure of an empty cyst.

Peer review

This paper describes the beneficial effect of *Da Cheng Qi* Decoction and Glauber's salt on ACS in SAP patients. Although the medication could not significantly improve the prognosis of SAP patients complicated by ACS, the data are encouraging and provide an important new clue to the treatment of ACS in SAP patients.

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