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CLINICAL STUDY

Modified Dachengqi Tang improves decreased gastrointestinal motility in postoperative esophageal cancer patients

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Abstract

OBJECTIVE: To investigate the clinical effects of modified Dachengqi Tang (DCQT) on promoting gastrointestinal motility in post-operative esophageal cancer patients.

METHODS: Sixty postoperative esophageal cancer patients were enrolled and randomly assigned to the modified treatment group or the control group (30 patients in each group). Patients in the treatment group were given DCQT made from decocted herbs and administered via nasojejunal tube at a dosage of 150 mL. Gastrointestinal motility was assessed by recording time for recovery of bowel sounds, flatus, defecation, and the total amount of gastric drainage during the first three postoperative days. Plasma motilin (MTL) and vasoactive intestinal peptide (VIP) were measured one hour before and three days after surgery.

RESULTS: Compared with the control group, the times to first bowel sound, flatus, and defecation were significantly shorter and there was less gastric drainage in the treatment group ($P < 0.01$, $P < 0.01$, $P < 0.01$, and $P < 0.05$, respectively). In the treatment group, postoperative plasma MTL was significantly higher ($P < 0.01$) and VIP was significantly lower than those in the control group ($P < 0.05$). There was no difference found in either MTL or VIP from before to after operation in the treatment group ($P > 0.05$). MTL was significantly lower and VIP was higher postoperatively in the control group, compared to before surgery ($P < 0.01$).

CONCLUSION: Modified DCQT effectively improved decreased gastrointestinal motility in postoperative esophageal cancer patients by increasing MTL and reducing VIP.

Key words: Dachengqi Tang; Esophageal neoplasms; Gastrointestinal motility; Nasojejunal infusion

INTRODUCTION

Esophageal cancer is a common malignancy, and the morbidity is increasing yearly. Each year about 200 000

people die from esophageal cancer, which makes it the eighth leading cause of morbidity and sixth leading cause of mortality worldwide.[1] Early surgery is the main treatment for esophageal cancer. However, it tends to induce temporary gastrointestinal dysfunction which is characterized by abdominal distension, belly-ache, nausea, vomiting, weak bowel sounds, and delayed defecation. In some cases, acute gastroparalysis and paralytic ileus may occur, which might result in death. Lee *et al* [2] reported that 50% of esophagectomy patients showed significantly delayed gastric emptying in the early stage after surgery. These disorders prolong recovery, increase discomfort, and increase hospitalization costs because of additional recovery days.[3] Therefore, promoting gastrointestinal motility after surgery in affected patients is important to decreasing complications and improving prognosis. The etiology of post-operative gastrointestinal dysfunction is unclear and attributed to multiple mechanisms. The mechanisms may include inhibitory sympathetic input,[4] injury or disconnection of the vagus nerve,[5] release of hormones[6] or neurotransmitters,[4] effects of anesthesia or analgesics,[7,8] negative pressure in the thoracic cavity, psychological stress like anxiety and tension,[9-11] or inflammatory reactions.[12] Various methods have been used to promote gastrointestinal motility in the clinical setting without much success. The current management for gastrointestinal motility recovery after esophageal cancer surgery uses Western Medicine, includes: routine postoperative indwelling stomach tube; continuous gastrointestinal decompression; fasting; postoperative nutritional support; gastric lavage with a warm saltwater solution; and, use of prokinetic agents. However, the treatments are often expensive and have frequent complications. Therefore, mild and economical Traditional Chinese Medicine (TCM) that can promote the recovery of gastrointestinal function are being increasingly studied.

Dachengqi Tang (DCQT), first documented in the classical TCM pharmacopoeia Treatise on Fevers,[13] is an herbal prescription composed of four component herbs or minerals: Dahuang (*Radix Et Rhizoma Rhei Palmati*), Mangxiao (*Nalrii Sulfas*), Houpu (*Cortex Magnoliae Officinalis*), and Zhishi (*Fructus Aurantii Immaturus*). DCQT has been used to treat gastrointestinal disorders for more than a thousand years. This study aimed to investigate the clinical effects and the mechanisms of nasojejunal infused DCQT on gastrointestinal motility in post-operative esophageal cancer patients.

MATERIALS AND METHODS

Patients

Patients were recruited from the Thoracic Surgery Department of Shandong Provincial Tumor Hospital. Patients who met all the following criteria were recruited in this study: age range from 18 to 75 years old; confirmed diagnosis and resection of esophageal cancer according to NCCN guidelines;[14] enteral nutrition being given via a nasal feeding tube after surgery; and compliance to treatment. Those who met one of the following criteria were excluded: an existing intestinal anastomosis after surgery; allergies; poor compliance, indicated by taking less than 80% or more than 120% of the prescribed medication; or receiving medicine or other treatment promoting gastrointestinal function. Sixty patients from March to July 2010 were selected and consecutively numbered according to their admission time. Patients were randomly divided into a treatment and control group with 30 patients in each according to a random number table. In the treatment group, there were 23 males and 7 females with a mean age of (60 ± 3) years (range 49 to 67 years). In the treatment group, 9 patients underwent intrathoracic anastomosis and 21 underwent cervical anastomosis. In the control group, there were 24 males and 6 females with a mean age of (60 ± 7) years (range 42 to 77 years). The control group had 6 patients that underwent intrathoracic anastomosis and 24 that underwent cervical anastomosis. There were no significant differences between the treatment and control groups in sex, age, or surgical approach. This clinical study was approved by the Medical Ethics and Human Clinical Trial Committee, and was conducted in accordance with the guidelines of the Declaration of Helsinki. All participants were clearly informed and consented.

Preparation of modified DCQT

A single dosage of modified DCQT consisted of Dahuang (*Radix Et Rhizoma Rhei Palmati*) 10 g, Mangxiao (*Nalrii Sulfas*) 5 g, Houpu (*Cortex Magnoliae Officinalis*) 15 g, Zhishi (*Fructus Aurantii Immaturus*) 15 g, Danggui (*Radix Angelicae Sinensis*) 15 g, Huangqi (*Radix Astragali Mongolici*) 15 g, Chishao (*Radix Paeoniae Rubra*) 15 g, and Wuyao (*Radix Linderae Aggregatae*) 10 g. The air-dried herbs were purchased from the Pharmacy Department of the Affiliated Hospital of Shandong University of Traditional Chinese Medicine (Shandong, China). All herbs except Mangxiao (*Nalrii Sulfas*) were soaked in 500 mL cold water for 1 h. The rhubarb was soaked separately. Herbs were decocted with gentle heat for 15 min. Then, rhubarb and 200 mL cold water were added and filtered to yield the decoction. Finally, the Mangxiao (*Nalrii Sulfas*) was dissolved in the decoction and the solution was concentrated. The final yield of the prepared decoction was 150 mL, which was stored in a sterile package at 4 ℃.

Treatments

All patients received esophageal cancer resection and esophagus-stomach anastomosis (intrathoracic anastomosis or cervical anastomosis). After surgery, all patients were given routine therapies, including fasting, gastrointestinal decompression, antibiotics, and enteral nutrition. Each patient in the treatment group was giv-

en a daily single dose of 150 mL DCQT on the morning of the first, second, and third day after the first enteral nutrition was provided 24 h after surgery. The decoction was infused through a nasojejunal feeding tube at 37 ℃ with the infusing thermostat at a speed of 80-100 drops per minute. The same regimen was followed in the controls, except that modified DCQT was replaced by 150 mL normal saline. No other medication affecting gastrointestinal motility was given to either group. During the infusion, all patients were closely observed for any adverse effects such as diarrhea, bellyache, or abdominal distention.

Experimental methods

The time to restoration of flatus, defecation, and intestinal sounds after surgery were recorded. The intestinal sound restoration was defined as at least three clear bowel sounds per minute calculated by a three-minute-long auscultation every 2 h. The total amount of gastric drainage in the 3 days after surgery was measured. The plasma concentrations of motilin (MTL) and vasoactive intestinal peptide (VIP) were measured by taking fasting venous blood samples 1 h before and 3 days after surgery (on the morning of the fourth day) separately with test tubes containing 40 μL of trasylol and 30 μL Na_2-ethylene diamine tetraacetic acid (EDTA). The samples were centrifuged immediately at 3000 rpm (1500 ×*g*) and 4 ℃ for 10 min and the separated serum was stored at - 80 ℃ for subsequent analysis. Before measurement, the cryopreserved plasma was thawed at room temperature and centrifuged at 3000 rpm and 4 ℃ for 5 min for radioimmunoassay with an intelligence γ-radioimmunoassay measuring instrument. The radioimmunoassay kit was supplied by the Beijing Puerweiye Biotechnology Company (Beijing, China). The SN-695B intelligence γ-radioimmunoassay apparatus was produced in the First Ring Instrument Factory affiliated to Shanghai Institute of Nuclear Research (Shanghai, China).

Statistical analysis

SPSS 13.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Data were expressed as mean ± standard deviation ($\bar{x} \pm s$). *T*-tests were conducted for differences between groups. $P < 0.05$ was considered significant.

RESULTS

The restoration of flatus, defecation, and intestinal sounds in the treatment group occurred much more quickly than those in the control group ($P < 0.01$, Table 1). There was significantly less total drainage in the treatment group than that in the control group ($P < 0.05$, Table 1). Among all the participants, only one woman in the treatment group had diarrhea on the end of the fourth day, which recovered quickly after discontinuing therapy.

There was no significant difference in preoperative plasma MTL or VIP concentrations between the treatment and control groups (both $P > 0.05$). The postoperative MTL was significantly higher and postoperative VIP was significantly lower in the treatment group compared with the control group ($P < 0.01$, $P < 0.05$). No significant differences in MTL or VIP were found from before to after surgery within the treatment group (both $P > 0.05$). However, the postoperative MTL was significantly lower and VIP was significantly higher than preoperative values in the control group (both $P < 0.05$) (Table 2).

DISCUSSION

According to TCM theory, decreased gastrointestinal motility in postoperative esophageal cancer patients results from *Qi* and blood stagnation and disordered *Zang* and *Fu* organs (i.e. lung, spleen, kidney, heart, stomach, small intestine, and large intestine). Therefore, TCM treatment aims to remove stasis to promote the flow of *Qi* and activate blood circulation, restore the *Zang* and Fu organs, and purge and dispel toxins and excess heat. DCQT is mainly composed of Dahuang (*Radix Et Rhizoma Rhei Palmati*), Mangxiao (*Nalrii Sulfas*), Houpu (*Cortex Magnoliae Officinalis*), and Zhishi (*Fructus Aurantii Immaturus*). The decoction aims to unblock interior *Qi* and purge heat to improve bowel movement. The Dahuang (*Radix Et Rhizoma Rhei Palmati*)[15-17] and Mangxiao (*Nalrii Sulfas*)[18] dispel excess internal heat and toxins, soften hard masses, and purge and cleanse the gastrointestinal tract. However, postoperative esophageal cancer patients tend to be weak and deficient in both *Qi* and blood, so catharsis should be mild. Therefore, we lowered the ca-

Table 1 Postoperative clinical indicators among the two groups ($\bar{x} \pm s$)

Indicator	Treatment group (*n*=30)	Control group (*n*=30)
Time to first flatus (h)	58±8	65±6
Time to first defecation (h)	97±10	113±12
Time to bowel sounds restoration (h)	34±6	43±7
Total gastric drainage (mL)	643±187	777±229

Notes: control group was treated with routine therapies (fasting, gastrointestinal decompression, antibiotics, and enteral nutrition); treatment group was given a daily single dose of 150 mL modified Dachengqi Tang on the morning of the first, second, and third day after the first enteral nutrition was provided 24 h after surgery.

Table 2 Pre- and post-operative plasma MTL and VIP (ng/L, $\bar{x} \pm s$)

Plasma concentration	Treatment group (n=30)	Control group (n=30)
Preoperative MTL	334±70[a]	387±85
Postoperative MTL	322±78[b,e]	230±60[g]
Preoperative VIP	159±29[c]	163±26
Postoperative VIP	175±34[d,f]	200±43[h]

Notes: control group was treated with routine therapies (fasting, gastrointestinal decompression, antibiotics, and enteral nutrition); treatment group was given a daily single dose of 150 mL modified Dachengqi Tang on the morning of the first, second, and third day after the first enteral nutrition was provided 24 h after surgery. MTL: motilin; VIP: vasoactive intestinal peptide. Independent-sample *t*-test: [a]P > 0.05, *vs* the preoperative control group, [b]P < 0.01, *vs* the postoperative control group. Independent-sample *t*-test: [c]P > 0.05 *vs* the preoperative control group. Paired-sample *t*-test: [d]P < 0.05 *vs* the postoperative control group. Paired-sample *t*-test: [e]P > 0.05 *vs* the preoperative treatment group, [g]P < 0.01 *vs* the preoperative control group. Paired-sample *t*-test: [f]P > 0.05 *vs* the preoperative treatment group, [h]P < 0.01 *vs* the preoperative control group.

thartic drugs Dahuang (*Radix Et Rhizoma Rhei Palmati*) from12 to 10 g and Mangxiao (*Nalrii Sulfas*) from 9 to 5 g. DCQT also includes Houpu (*Cortex Magnoliae Officinalis*) to promote *Qi* circulation, eliminate dampness, and relieve dyspepsia. Zhishi (*Fructus Aurantii Immaturus*) eliminates phlegm and stasis,[19] and Danggui (*Angelica sinensis*) nourishes and activates blood, relieves pain, and lubricates and tonifies the intestine. Huangqi (*Radix Astragali Mongolici*) is added to DCQT for *Qi* tonification and *Yang* lifting.[20] Chishao (*Radix Paeoniae Rubra*) is added to clear heat, cool blood, and eliminate stasis to alleviate pain.[21] Finally, Wuyao (*Radix Linderae Aggregatae*) is used to promote *Qi* circulation and relieve pain.[22,23] In addition to the pharmacological effect of the herbs, the monosaccharides, polysaccharides, and electrolytes contained in the decoction also provide nutrients for the gastrointestinal mucosa. Overall, DCQT unblocks interior *Qi* and nourishes the *Zang* and *Fu* organs, particularly for those who have just underwent major surgery.

We found that DCQT dramatically improved patient postoperative condition as demonstrated by clinical symptoms and laboratory indexes. Flatus, defecation, and intestinal sounds were restored much more quickly in the treatment group than in the control group. Meanwhile, there was significantly less gastric drainage in the treatment group compared with the control group. Therefore, modified DCQT improved gastrointestinal motility after surgery, which is consistent with other studies.[24-27] Among all treatment patients, only one woman had diarrhea on the fourth day, which recovered soon after discontinuing DCQT treatment. This suggests that DCQT treatment is relatively safe, but the specific dosage for individuals should be further investigated.

Gastrointestinal motility is modulated by several hormones. MTL, a polypeptide hormone containing 22 amino acids, is secreted by endocrine M cells and acts at motilin receptors to promote gastrointestinal motility by stimulating migrating myoelectric complex phase Ⅲ and pepsin production.[28-30] Studies have shown that motilin receptor agonists ameliorated functional dyspepsia by increasing the level of plasma motilin.[31,32] Lu *et al* [33] found that plasma MTL levels in preoperative esophageal cancer patients were higher compared with normal people, and MTL levels increased gradually with the development of cancer. In this study, no differences in MTL levels were found between esophageal cancer patients and healthy patients. This may be because patients had earlier stage esophageal cancer, or the small sample size was too small. Experimental results indicate that the postoperative level of plasma MTL was significantly higher in the treatment group than that in the control group, but there was no significant difference between the two groups preoperatively. The postoperative level of MTL was significantly lower than the preoperative level in the control group but not the treatment group. These MTL results indicate that gastrointestinal motility recovered earlier in the treatment group.

VIP, a 28-amino acid polypeptide acting at G-protein-coupled receptors in the gastrointestinal tract,[34] induces intestinal smooth muscle relaxation, stimulates water and bicarbonate secretion, and inhibits secretion of gastric acid and pepsin.[35] One animal study found that VIP has an inhibitory effect on gastrointestinal motility and gastric emptying.[29] In this study, VIP was significantly lower in the treatment group compared with the control group postoperatively while there was no significant difference between the two groups preoperatively. The level of plasma VIP was significantly higher after surgery in the control group but not the treatment group. Therefore, postoperative gastrointestinal motility was suppressed in the control group, but not the treatment group. DCQT promoted gastrointestinal motility after esophageal cancer resection by improving MTL and reducing VIP, which is in accordance with previous study.[36]

Studies have shown that there are various approaches for DCQT administration, including oral administration, enema, or nasal feeding.[27,37-41] We found that nasal feeding via nasojejunal tube may be superior because of higher tolerance, lower risk of reflux, and faster absorption.

DCQT significantly promoted gastrointestinal motility in postoperative esophageal cancer patients by improv-

ing MTL and reducing VIP. However, the sample size was small. More research at the molecular level should be performed to study the mechanism, determine appropriate DCQT dosages, and evaluate the safety of this decoction.

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REFERENCES

1 **Hongo M**, Nagasaki Y, Shoji T. Epidemiology of esophageal cancer: orient to occident. effects of chronology, geography and ethnicity. J Gastroenterol Hepatol 2009; 24(5): 729-735.
2 **Lee HS**, Kim MS, Lee JM, Kim SK, Kang KW, Zo JI. Intrathoracic gastric emptying of solid food after esophagectomy for esophageal cancer. Ann Thorac Surg 2005; 80 (2): 443-447.
3 **Moss G**, Regal ME, Lichtig LK. Reducing postoperative pain, narcotics, and length of hospitalization. Surgery 1986; 99(2): 206-210.
4 **Livingston EH**, Passaro EP Jr. Postoperative ileus. Dig Dis Sci 1990; 35(1): 121-132.
5 **Yokota M**, Ando N, Ozawa S, Imazu Y, Kitajima M. Enhanced motility of the vagotomized canine stomach by electrical stimulation. J Gastroenterol Hepatol 1997; 12 (4): 338-346.
6 **Beglinger C**, Ddegen L. Role of thyrotrophin releasing hormone and corticotrophin releasing factor in stress related alterations of gastrointestinal motor function. Gut 2002; 51(Suppl Ⅰ): 145-149.
7 **Wilder-Smith CH**, Hill L, Wilkins J, Denny L. Effects of morphine and tramadol on somatic and visceral sensory function and gastrointestinal motility after abdominal surgery. Anesthesiology 1999; 91(3): 639-647.
8 **Moraca RJ**, Sheldon DG, Thirlby RC. The role of epidural anesthesia and analgesia in surgical Practice. Ann Surg 2003; 238(5): 663-673.
9 **Mu ZB**, Huang YX. Research status of the relationship between psychological stress and gastrointestinal motility. Zhong Guo Zong He Lin Chuang 2005; 21(5): 473-475.
10 **Rao SS**, Hatfield RA, Suls JM. Psychological and physical stress induce differe ntial effects on human colonic motility. Am J Gastroenterol 1998; 93(6): 985-990.
11 **Hao Y**, Huang YX, Wang JJ. Effect of psychological stress on gastric emptying and gastricmucosal lesions in rats. Di Si Jun Yi Da Xue Xue Bao 2002; 23(7): 603-605.
12 **Kalf JC**, Schraut WH, Billiar TR, Simmons RL, Bauer AJ. Role of inducible nitric oxide synthase in postoperative intestinal smooth muscle dysfunction in rodents. Gastroenterology 2000; 118(2): 316-327.
13 **Zhang ZJ** (Han dynasty), Yang PJ. Treatise on fevers. Beijing: Academy Press, 2013: 77.
14 **Ben XS**, Wang MT, Zhou ZH, translators. NCCN esophageal neoplasms practice guidelines. J Evid-Based Med 2008; 8(6): 360-373.
15 **Li F**, Wang SC, Wang X, et al. Novel exploration of cathartic pharmacology induced by rhubarb. Zhong Guo Zhong Yao Za Zhi 2008; 33(4): 481-484.
16 **Tseng SH**, Lee HH, Chen LG, Wu CH, Wang CC. Effects of three purgative decoctions on inflammatory mediators. J Ethnopharmacol 2006; 105(1-2): 118-124.
17 **Tseng SH**, Chien TY, Tzeng CF, Lin YH, Wu CH, Wang CC. Prevention of hepatic oxidative injury by Xiaochenchi Tang in mice. J Ethnopharmacol 2007; 111(2): 232-239.
18 **Patel V**, Nicar M, Emmett M, et al. Intestinal and renal effects of low-volume phosphate and sulfate cathartic solutions designed for cleansing the colon: pathophysiological studies in five normal subjects. Am J Gastroenterol 2009; 104(4): 953-965.
19 **Gao L**, Wang J, Li F, Gao S, Deng Y. Analysis on clinically drug-used law for lung-intestine related diseases. J Tradit Chin Med 2012; 32(4): 523-528.
20 **Wang H**, Zhang Y, Xia T, et al. Synergistic promotion of blood vessel regeneration by astragaloside IV and ferulic acid from electrospun fibrous mats. Mol Pharm 2013; 10 (6): 2394-3-2403.
21 **Liu Y**, Yin H, Jiang Y, et al. Correlation between platelet gelsolin and platelet activation level in acute myocardial infarction rats and intervention effect of effective components of chuanxiong rhizome and red peony root. Evid Based Complement Alternat Med 2013; 2013: 985746.
22 **Luo Y**, Liu M, Xia Y, Dai Y, Chou G, Wang Z. Therapeutic effect of norisoboldine, an alkaloid isolated from Radix Linderae, on collagen-induced arthritis in mice. Phytomedicine 2010; 17(10): 726-731.
23 **Li Q**, Chou G, Dou C, Wang Z, Huang F. Studies on the analgesic and antiinflammatory action of radix Linderae extract. Zhong Yao Cai 1997; 20(12): 629-631.
24 **You SY**, Wu CZ, Liu ML. Effects of Dachengqi decoction on gut hormones and intestinal movement after cholecystomy. Zhong Guo Zhong Xi Yi Jie He Za Zhi 1994; 14 (9): 522-524.
25 **Qi QH**, Wang J, Liang GG, Wu XZ. Dachengqi Tang promotes the recovery of gastrointestinal motility after abdominal surgery in humans. Dig Dis Sci 2007; 52(6): 1562-1570.
26 **Cao BL**, Jiao L, Liu XM. Application of Dachengqi granule in the perioperative period of total laparoscopic hysterectomy. Zhong Guo Zhong Xi Yi Jie He Za Zhi 2009; 29 (5): 441-443.
27 **Wang J**, Liu H, Qi QH. Effect of Dachengqi Tang on gastrointestinal motility in patients undergoing laparotomy. Hepato-gastroenterology 2011; 58(112): 1887-1892.
28 **Miller P**, RoyA, St-Pierre S, Dagenais M, Lapointe R, Poitras P. Motilin receptors in the human antrum. Am J Physiol Gastrointest Liver Physiol 2000; 278(1): G18-G23.
29 **Ljung T**, Hellstriom PM. Vasoactive intestinal peptide suppresses migrating myoelectric complex of rat small intestinal independent of nitric oxide. Acta Phsiol Scand 1999; 165(2): 225-231.
30 **Van-Assche G**, Depoortere I, Thijs T, et al. Contractile effects and intracellular Ca^{2+} signalling induced by motilin and erythromycin in circular smooth muscle of human

colon. Neurogastroenterol Motil 2001; 13(1): 27-35.

31 **Ozaki K**, Yogo K, Sudo H, et al. Effects of mitemcinal (GM-611), an acid-resistant non-peptide motilin receptor agonist on the gastrointestinal contractile activity in conscious dogs. Pharmacology 2007; 79(4): 223-235.

32 **Yogo K**, Onoma M, Ozaki M, et al. Effects of oral mitemcinal (GM-611), erythromycin, EM-574 and cisapride on gastric emptying in conscious Rhesus monkeys. Dig Dis Sci 2008; 53(4): 912-918.

33 **Lu ZT**, Sun WJ, Sun GW, Luo NP, Liu GL. The dynamic observation and clinical significance of plasma motilin in postoperative esophagus cancer and cardiac carcinoma of the aged. Chin J Geriatr 1997; 16(3): 132.

34 **Moody TW**, Ito T, Osefo N, Jensen RT. VIP and PACAP: recent insights into their functions/roles in physiology and disease from molecular and genetic studies. Curr Opin Endocrinol Diabetes Obes 2011; 18(1): 61-67.

35 **Igarashi H**, Fujimori N, Ito T, et al. Vasoactive intestinal peptide (VIP) and VIP receptors-elucidation of structure and function for therapeutic applications. Int J Clin Med 2011; 2(4): 500-508.

36 **Li Y**, Tian TY, Ma ZL, Huang BM, Cheng YA. The effect of Dachengqi decoction on gut hormone externalization and promoting gastrointestinal motility. Henan Zhong Yi Xue Yuan Xue Bao 2008; 23(5): 19-21.

37 **Yang SL**, Li DB. Clinical study on therapy of clearing hallow viscera in treating critical patients with gastro-enteric function disorder. Chin J Integr Med 2006; 12(2): 122-125.

38 **Zhang MJ**, Zhang GL, Yuan WB, Ni J, Huang LF. Treatment of abdominal compartment syndrome in severe acute pancreatitis patients with Traditional Chinese Medicine. World J Gastroenterol 2008; 14(22): 3574-3578.

39 **Ren YY**, Gong HL, Tang WF, Wan MF, Huang X. Effects of ranitidine on pharmacokinetics of rhein from Dachengqi decoction in rats after oral administration. Zhong Xi Yi Jie He Xue Bao 2009; 7(9): 868-872.

40 **Chen H**, Li F, Jia JG, Diao YP, Li ZX, Sun JB. Effects of Traditional Chinese Medicine on intestinal mucosal permeability in early phase of severe acute pancreatitis. Chin Med J 2010; 123(12): 1537-1542.

41 **Suo T**, Gu XX, Andersson R, et al. Oral traditional Chinese medication for adhesive small bowel obstruction. Cochrane Database Syst Rev 2012; 16(5): CD008836.