

DA-CHENG-QI DECOCTION, A TRADITIONAL CHINESE HERBAL FORMULA, FOR INTESTINAL OBSTRUCTION: SYSTEMATIC REVIEW AND META-ANALYSIS

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Abstract

Background: This study was aimed at determining the effects and safety of Da-Cheng-Qi decoction (DCQD) or DCQD combined with conservative therapy in patients with intestinal obstruction.

Materials and Methods: PubMed, EMBASE, Cochrane Controlled Trials Register, and several other databases were searched. Randomised controlled trials (RCTs) of DCQD or DCQD plus conservative therapy in patients with intestinal obstruction were eligible. Therapeutic effect was estimated by the improvement of clinical manifestations and diagnostic imaging; dichotomous/ordinal data assessment of overall response to therapy, adverse effects; or continuous variable were identified, including time to first bowel movement, time to first flatus, length of hospital stay.

Results: Sixty eligible RCTs including 6,095 patients were identified. Response rate: (1) DCQD versus conservative therapy (6 RCTs, 361 patients, RR of respond =1.13; 95% CI 0.97 to 1.31). (2) DCQD plus conservative therapy versus conservative therapy (48 RCTs, 4,916 patients, RR of respond =1.25 which favoured DCQD plus conservative therapy; 95% CI 1.20 to 1.30). Treatment effect remained similar when RCTs at high risk of bias were excluded. Time to first flatus postoperatively: (1) DCQD versus conservative therapy (2 RCTs, 240 patients, SMD=-3.65; 95% CI -8.17 to 0.87). (2) DCQD plus conservative therapy versus conservative therapy (11 RCTs, 1,040 patients, SMD=-2.09 which favoured DCQD plus conservative therapy; 95% CI -3.04 to -1.15).

Conclusion: DCQD combined with conservative therapy may increase the success rate of conservative therapy for intestinal obstruction significantly and can shorten the duration of postoperative ileus in patients undergoing abdominal surgery compared with conservative therapy alone.

Key words: Da-Cheng-Qi-Tang; Intestinal Obstruction; Ileus; Intestinal Pseudo-Obstruction; Meta-Analysis.

Introduction

Intestinal obstruction refers to any impairment, arrest, or reversal of the normal flow of intestinal contents toward the anal canal. It can be classified according to pathogenesis: ileus (a transient impairment of bowel motility caused by operation, inflammation, metabolism, neurogenic reasons and drugs) and mechanical intestinal obstruction (a kind of obstruction caused by any mechanical reasons, such as adhesion, neoplasm or herniation. And it accounts for approximately 15% of all emergency department visits for acute abdominal pain (Williams et al., 2005)). Postoperative ileus and mechanical intestinal obstruction caused by postoperative adhesions are the predominant types respectively. (Moran, 2007; Kumar et al., 2009) For ileus, conservative therapy containing bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics and sometimes cathartics are the main strategies of treatment. As for mechanical intestinal obstruction, surgery is warranted in patients with obstruction when conservative therapy does not resolve within 48 hrs after it initiated (Fevang et al., 2002). Conservative therapy has been shown to be successful in more than 70% of the patients with mechanical intestinal obstruction (Tanaka et al., 2008). However, delay in diagnosis and suitable treatment may cause a substantial increase of complications. The complications of intestinal obstruction include bowel ischemia and perforation, which may lead to severe outcomes or even death. (Markogiannakis et al., 2007) The diagnosis and treatment of intestinal obstruction remains a challenge.

Da-Cheng-Qi decoction (DCQD), Dai-joki-to in Japanese, a classic Chinese herbal formula (Satoh, 2013), is commonly used for the treatment of intestinal obstruction besides modern medicine in Chinese hospitals (Qi et al, 2004). The main components of DCQD are *Radix et Rhizoma*

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Rhei, *Cortex Magnoliae Officinalis*, *Fructus Aurantii Immaturus* and *Natrii Sulfas*. Herbs in formula can sometimes be slightly adjusted (*jiajian* in Chinese pinyin) by doctor's judgments about the patients' clinical manifestations. DCQD can be administered via oral or rectal, and is to be stopped if patients egrets. Though pharmacological studies have shown different positive effects of the single plant extracts in DCQD, (Xu et al., 2010; Tang et al., 2008; Qi et al., 2007; Gong et al., 2011) as a formula, efficacy or side-effects of DCQD has not been systematically assessed till now. Therefore, the objective of the systematic review and meta-analysis is to determine the effects (benefits and harms) of DCQD in the treatment of intestinal obstruction, in mono-therapy or in combination with conservative therapy, as compared to conservative therapy alone.

Methods

Search strategy and study selection.

A search of the medical literature was conducted using PubMed (up to July 2011), EMBASE (1980 to July 2011), Cochrane Controlled Trials Register (issue 7, 2011), Sinomed (up to July 2011), China National Knowledge Infrastructure (CNKI) database (1994 to July 2011), Wanfang Data (1989 to July 2011) and the VIP Information (1990 to July 2011). Randomised Controlled Trials (RCTs) comparing the effects of DCQD or DCQD plus conservative therapy with conservative therapy in adult patients with intestinal obstruction (ileus or mechanical) were eligible for inclusion. Trials using other pharmaco-therapies were eligible, as long as these were administered to both the intervention and control groups. Diagnosis of intestinal obstruction could be based on case history, clinical manifestations and diagnostic imaging (X-ray or computed tomography scan). The primary outcome of this meta-analysis was estimated by the improvement of clinical manifestations (relief of abdominal pain, passage of flatus/stool, bowel movement) and diagnostic imaging (X-ray or computed tomography scan). We attempted to contact the original investigators in order to obtain further information if necessary. Studies on intestinal obstruction were identified with the terms *intestinal obstruction*; *intestinal pseudo-obstruction* and *ileus*, (both as medical subject heading (MeSH) and free text terms), *small bowel obstruction*, *SBO* and *large bowel obstruction* (as free text terms). These were combined using the set operator AND, with studies identified using the terms: *Da-Cheng-Qi-Tang*, *DCQT herbal medicine* and *Drugs, Chinese Herbal* (MeSH terms), *Da-Cheng-Qi decoction* (free text terms). We also searched the reference lists of the original reports, reviews, letters to the editor, case reports and meta-analyses of studies involving Chinese herbal medicine (retrieved through the electronic searches) to identify studies which had not yet been included in the computerised databases, all potentially relevant papers were obtained and evaluated in detail. There were no language restrictions. Articles were independently assessed by two reviewers (YB and XFY) using predesigned eligibility criteria: 1) randomised controlled trials; 2) diagnosis of intestinal obstruction based on case history, clinical manifestations and diagnostic imaging (X-ray or computed tomography scan); 3) interventions: DCQD or DCQD plus conservative therapy compared with conservative therapy (DCQD *jiajian* was allowed); 4) decoction administered via oral and/or rectal; 5) therapeutic effect was estimated by the improvement of clinical manifestations (relief of abdominal pain, passage of flatus/stool, bowel movement) and/or diagnostic imaging (X-ray or computed tomography scan); 6) dichotomous/ordinal data assessment of overall response to therapy, adverse effects; or continuous variable were identified, including time to first flatus, time to first bowel movement, length of hospital stay. Any disagreement between reviewers was resolved by consensus between the two reviewers (YB and XFY), adjudicated with the support of a third reviewer (SHJ).

Outcome assessment

The primary outcome assessed was the obstruction cured or improvement at the end of treatment. Failure to response to therapy was defined as no improvement in clinical manifestations (ileus) or as needing surgical treatment (mechanical). If ordinal data were given to define obstruction improvement, they were transformed into dichotomous data (e.g. if the scale was 1, no improvement (ileus) or needs surgical treatment (mechanical); 2, a little improvement; 3, a moderate amount of improvement; 4, great improvement; the latter 3 descriptors were defined as positive outcomes). Secondary outcomes considered was continuous data defined as time to first flatus.

Data extraction

All data were extracted independently by two reviewers (Y.B. and SHJ) onto a pre-designed form (Microsoft Office Excel 2007; Microsoft Corp, Redmond, Washington, USA). All data extraction was then checked by a third reviewer (ZZ). The following data were extracted for each trial: number of centres; geographical location of the study; study population; sample size; proportion of female patients; criteria used to define

intestinal obstruction; aetiology (including detailed abdominal operation histories); the route of administration; duration of treatment; concomitant medications allowed; total number of adverse events reported; primary outcome measure used to define clinical manifestations improvement or cure following treatment; duration of follow-up; method used to generate the randomization schedule and conceal allocation. Data were extracted as intention-to-treat analyses, where all drop-outs were assumed to be treatment failures, wherever trial reporting allowed this.

Assessment of risk of bias

Assessment of risk of bias was performed independently by two reviewers (YB and SHJ), with disagreements resolved by discussion. Risk of bias was assessed according to the elaborated CONSORT checklist for herbal interventions (Gagnier et al., 2006, 2006) by recording characteristics of the herbal product, qualitative testing, dosage regimen and quantitative description, method used to generate the randomization schedule and conceal allocation, whether blinding was implemented, what proportion of patients completed follow-up, and whether an intention-to-treat analysis was extractable etc.. 2-properly with detailed description, 1-mentioned but not detailed reported, 0-not mentioned or inappropriate. A trial with a quality score ≤ 18 was considered as a trial at high risk of bias, and a trial with a quality score ≥ 36 was considered as a trial at low risk of bias, the left were at moderate risk of bias.

Data synthesis and statistical analysis

Data were pooled using a random effects model to produce wider confidence intervals and more conservative estimates.(DerSimonian et al., 1986) The impacts of DCQD on dichotomous outcomes were expressed as a relative risk (RR) of response to therapy with intervention compared with control with 95% confident intervals (CIs). The number needed to treat (NNT) with 95% CIs were calculated from the reciprocal of the risk difference of the meta-analysis. Time to first flatus was examined using a standardised mean difference (SMD) with a 95% CI.

Heterogeneity between studies was assessed using the I^2 statistic with a cut-off of $> 50\%$ to define a significant degree of heterogeneity. We conducted a pre-specified sensitivity analyses according to the type of intestinal obstruction, risk of bias of identified trials, detailed operation histories, the route of administration and the definition of response to therapy. These were exploratory analyses only, and may explain some of the observed variability, the results, however, should be interpreted with caution.

Review Manager Version 5.0 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2008) and Stata/SE version 10.0 (StataCorp, College Station, Texas, USA), were used to generate forest plots for outcomes with 95% CIs, as well as funnel plots. The latter were assessed for evidence of asymmetry, and possible publication bias or other small study effects were evaluated using the Begg's test. (Begg et al., 1994)

Results

The search strategy initially yielded 752 citations, 109 of which appeared to be relevant to the systematic review and were retrieved for further assessment (Figure 1). Of these, 49 were excluded for various reasons, leaving a total of 60 eligible articles. Seven RCTs compared the effect of DCQD with conservative therapy, 54 compared the effect of DCQD plus conservative therapy with conservative therapy alone. Characteristics of the included trials were shown in supplementary Tables.

DCQD versus conservative therapy

The seven RCTs comparing DCQD with conservative therapy involved a total of 521 patients. Five trials were at moderate and two trials were at high risk of bias according to the modified elaborated CONSORT statement for herbal interventions. The pathogenesis in six RCTs was ileus while it was incomplete mechanical intestinal obstruction in one trial. Dichotomous data could be extracted from six RCTs. There were 24 (13.2%) of 182 patients assigned to DCQD who failed to respond to therapy, compared with 38 (21.2%) of 179 allocated to conservative therapy (RR of respond=1.13; 95% CI 0.97 to 1.31) (Fig 2). There was borderline heterogeneity between studies ($I^2=58\%$), with no statistically significant funnel plot asymmetry (Begg's test, $p=1.00$) suggesting no evidence of publication bias or other small study effects

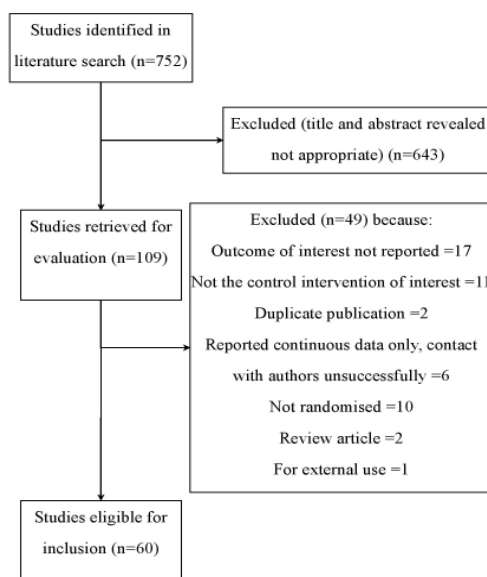


Figure 1: Flow diagram of RCTs included

Table 1: Sensitivity analyses of efficacy of DCQD in intestinal obstruction

| | <i>Number of studies</i> | <i>Number of subjects</i> | <i>RR</i> | <i>95% CI</i> | <i>I² value</i> | <i>NNT</i> | <i>95% CI</i> |
|--|--------------------------|---------------------------|-----------|---------------|----------------------------|------------|---------------|
| All studies# | 6 | 361 | 1.13 | 0.97 to 1.31 | 58% | N/A | N/A |
| Risk of bias of trials | | | | | | | |
| Moderate | 5 | 301 | 1.14 | 0.95 to 1.39 | 66% | N/A | N/A |
| High | 1 | 60 | 1.08 | 0.88 to 1.32 | N/A | N/A | N/A |
| Route of administration | | | | | | | |
| Via oral | 4 | 231 | 1.08 | 0.84 to 1.39 | 67% | N/A | N/A |
| Via rectal | 2 | 130 | 1.22 | 0.93 to 1.59 | 70% | N/A | N/A |
| Definition of response to therapy | | | | | | | |
| Clinical alone | 4 | 301 | 1.07 | 0.91 to 1.25 | 65% | N/A | N/A |
| Clinical + Imaging | 2 | 60 | 1.45 | 1.11 to 1.91 | 0% | 3.2 | 2 to 7.7 |
| Aetiology | | | | | | | |
| Postoperative | 3 | 190 | 1.15 | 1.01 to 1.31 | 35% | 7.7 | 4.2 to 50 |
| Non-postoperative | 3 | 171 | 1.11 | 0.72 to 1.73 | 78% | N/A | N/A |

N/A, not applicable; # refers to the studies dichotomous data can be extracted from.

Response to therapy in patients with ileus

The five trials studying ileus reported dichotomous data of 301 patients. Overall, ileus was caused by operation in 190 patients. 21 (13.8%) of 152 patients assigned to DCQD failed to respond to therapy compared with 33 (22.1%) of 149 patients allocated to conservative therapy (RR of respond =1.14; 95% CI 0.95 to 1.39). There was significant heterogeneity between studies ($I^2=66\%$) with no evidence of funnel plot asymmetry (Begg's test, $p=0.73$). Two RCTs reported continuous data of the time to first flatus post-operatively. There was no statistical difference when results of individual RCTs were combined (SMD=-3.65; 95% CI -8.17 to 0.87) (Figure 3), and there was significant heterogeneity among these two studies ($I^2=99\%$).

Response to therapy in patients with mechanical intestinal obstruction

Only one trial containing 60 patients studied incomplete mechanical intestinal obstruction, 3 (10.0%) of 30 patients assigned to DCQD failed to respond to therapy compared with 5 (16.7%) of 30 patients allocated to conservative therapy (RR of respond =1.08; 95% CI 0.88 to 1.32) (Figure 2).

Sensitivity analysis

Given the borderline heterogeneity observed when results of individual RCTs were combined, we conducted pre-specified sensitivity analyses (Table 1). The RR of respond was relatively stable in these analyses. Heterogeneity between trials was lower and 95% CI doesn't include the number "1" when only the two studies that used clinical manifestations and imaging improvement to define response to therapy were included in the analysis. Treatment effect remained similar when only the five trials at low risk of bias were considered.

DCQD plus conservative therapy versus conservative therapy

The 54 RCTs comparing DCQD plus conservative therapy with conservative therapy contained a total of 5,574 patients with intestinal obstruction. 27 trials were at moderate and 27 trials were at high risk of bias. Twenty-one RCTs studied ileus while 33 studied mechanical intestinal obstruction. Dichotomous data could be extracted from 48 RCTs. There were 221 (8.4%) of 2,641 patients assigned to DCQD plus conservative therapy who failed to respond to therapy, compared with 648 (28.5%) of 2,275 allocated to conservative therapy alone (RR of respond=1.25; 95% CI 1.20 to 1.30 which favoured DCQD plus conservative therapy), with borderline heterogeneity between studies ($I^2=55\%$) (Fig 4) and an NNT of 5.3 (95% CI 4.8 to 6.3). There was no statistically significant funnel plot asymmetry (Begg's test, $p=0.31$) suggesting no evidence of publication bias or other small study effects.

Response to therapy in patients with ileus

In the 21 trials studying ileus, 15 reported dichotomous data in 1,168 patients. Overall, ileus of 879 patients was caused by operation. Fifty-one (8.4%) of 606 patients assigned to DCQD plus conservative therapy failed to respond to therapy compared with 150 (26.7%) of 562 patients allocated to conservative therapy (RR of respond =1.23; 95% CI 1.13 to 1.34 which favoured DCQD plus conservative therapy) (Fig 4), with significant heterogeneity between studies ($I^2=67\%$) and an NNT of 5.9 (95% CI 4.3 to 9.1). There was no evidence of funnel plot asymmetry (Begg's test, $p=0.19$).

Eleven RCTs reported continuous data of time to first flatus post-operatively. There was statistical difference when results of individual RCTs were combined (SMD=-2.09; 95% CI -3.04 to -1.15 which favoured DCQD plus conservative therapy) (Fig 3), and there was significant heterogeneity among studies ($I^2=97\%$).

Table 2: Sensitivity analyses of efficacy of DCQD plus conservative therapy in intestinal obstruction

| | <i>Number of studies</i> | <i>Number of subjects</i> | <i>RR</i> | <i>95% CI</i> | <i>I² value</i> | <i>NNT</i> | <i>95% CI</i> |
|--|--------------------------|---------------------------|-------------|---------------------|----------------------------|------------|-------------------|
| All studies# | 48 | 4,916 | 1.25 | 1.20 to 1.30 | 55% | 5.3 | 4.8 to 6.3 |
| Risk of bias of trials | | | | | | | |
| Moderate | 23 | 1,996 | 1.24 | 1.16 to 1.33 | 69% | 5.6 | 4.5 to 7.7 |
| High | 25 | 2,920 | 1.26 | 1.21 to 1.31 | 18% | 5 | 4.3 to 5.9 |
| Route of administration | | | | | | | |
| Via oral | 22 | 2,231 | 1.22 | 1.16 to 1.28 | 33% | 5.9 | 5 to 7.7 |
| Via rectal | 12 | 1,072 | 1.32 | 1.24 to 1.39 | 0% | 4.2 | 3.6 to 5.3 |
| Oral and rectal | 14 | 1,613 | 1.24 | 1.13 to 1.36 | 77% | 5.6 | 4.2 to 9.1 |
| Definition of response to therapy | | | | | | | |
| Clinical alone | 11 | 1,136 | 1.30 | 1.19 to 1.41 | 48% | 4.8 | 3.7 to 6.3 |
| Clinical + Imaging | 37 | 3,780 | 1.24 | 1.18 to 1.29 | 55% | 5.6 | 4.8 to 6.7 |
| Aetiology | | | | | | | |
| Postoperative | 35 | 3,724 | 1.22 | 1.17 to 1.27 | 53% | 5.9 | 5 to 7.1 |
| Non-postoperative | 13 | 1,192 | 1.34 | 1.24 to 1.45 | 31% | 4.2 | 3.6 to 5 |

refers to the studies dichotomous data can be extracted from

Supplementary Table 1: Characteristics of the included RCTs (part A)

| trials | DOI | definition of intestinal obstruction | aetiology | clinical background | female patients | number of participants | average age | route of DCQD administration | duration of treatment | duration of follow-up |
|---------------------|-----------------------------------|--|------------|-----------------------------------|-----------------|------------------------|-------------|------------------------------------|-----------------------|-----------------------|
| Ao XR 2007 | CNKI:SUN:JXZY.0.2007-07-039 | diagnostic imaging + clinical manifestations | mechanical | abdominal surgery | 44 | 96 | 44.4 | (nasogastric tube/oral) and rectal | 5d | N/A |
| Cao SB 2008 | CNKI:SUN:SXZY.0.2008-09-031 | diagnostic imaging + clinical manifestations | ileus | N/A | 26 | 69 | 71.1 | rectal | 7d | N/A |
| Chen CQ 2002 | cnki:ISSN:1009-9727.0.2002-03-017 | clinical manifestations alone | ileus | stroke | 71 | 180 | 58.5 | nasogastric tube/oral | 14d | N/A |
| Chen H 2009 | CNKI:SUN:CZXX.0.2009-04-045 | diagnostic imaging + clinical manifestations | mechanical | N/A | 24 | 65 | 42.24 | nasogastric tube/oral | 78h | N/A |
| Chen ZJ 2004 | cnki:ISSN:1005-7331.0.2004-02-027 | clinical manifestations alone | mechanical | abdominal surgery | 15 | 50 | 50.8 | rectal | 5d | N/A |
| Dong ZC 2008 | CNKI:SUN:SXZY.0.2008-05-026 | diagnostic imaging + clinical manifestations | mechanical | abdominal surgery | 27 | 68 | 56.9 | (nasogastric tube/oral) and rectal | 10d | N/A |
| Dou WH 2009 | CNKI:SUN:SHIX.0.2009-07-019 | diagnostic imaging + clinical manifestations | mechanical | abdominal surgery | 34 | 80 | 41.8 | nasogastric tube/oral | 10d | N/A |
| Fan Y 2007 | CNKI:ISSN:1003-5699.0.2007-03-019 | clinical manifestations alone | mechanical | abdominal surgery | N/A | 60 | N/A | nasogastric tube/oral | 48h | N/A |
| Fang HL 2008 | CNKI:SUN:GAYX.0.2008-04-076 | diagnostic imaging + clinical manifestations | mechanical | abdominal surgery | 267 | 538 | N/A | (nasogastric tube/oral) and rectal | N/A | N/A |
| Fu HB 2008 | CNKI:SUN:BHON.0.2008-03-026 | diagnostic imaging + clinical manifestations | ileus | stroke | 27 | 62 | 63.5 | nasogastric tube/oral | 3d | N/A |
| Gao JC 2005 | cnki:ISSN:1000-3649.0.2005-01-017 | clinical manifestations alone | ileus | abdominal surgery | 12 | 42 | 39 | nasogastric tube/oral | 7d | 1y |
| Gao ZJ 2010 | CNKI:SUN:SXZY.0.2010-09-034 | diagnostic imaging + clinical manifestations | ileus | abdominal neoplasm or peritonitis | 15 | 60 | 51.75 | nasogastric tube/oral | 21d | N/A |
| He GM 2009 | CNKI:SUN:ZDYS.0.2009-21-060 | diagnostic imaging + clinical manifestations | mechanical | abdominal surgery | 50 | 97 | 40.6 | nasogastric tube/oral | 7d | N/A |
| Hu ZG | CNKI:SUN:HNZG.0.20 | diagnostic imaging + | mecha | N/A | 59 | 126 | 52.5 | (nasogastric | 48h | 1-5y |

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| | | | | | | | | | | |
|-----------------|------------------------|-------------------------|-------|-------------------|-----|-----|-------|------------------------------------|-----|--------|
| 2008 | 08-04-030 | clinical manifestations | nical | | | | | tube/oral) and rectal | | |
| Jiang CL | CNKI:SUN:HNZY.0.20 | diagnostic imaging + | mecha | abdominal surgery | 58 | 110 | 34.6 | rectal | N/A | N/A |
| 2008 | 08-07-048 | clinical manifestations | nical | | | | | | | |
| Jiang K | CNKI:SUN:LZXB.0.20 | diagnostic imaging + | ileus | abdominal surgery | 23 | 50 | 41.5 | rectal | N/A | N/A |
| 2009 | 09-04-071 | clinical manifestations | | | | | | | | |
| Li H | CNKI:SUN:GSZY.0.20 | diagnostic imaging + | ileus | abdominal surgery | 25 | 56 | 36.1 | nasogastric tube/oral | 7d | N/A |
| 2010 | 10-05-015 | clinical manifestations | | | | | | | | |
| Li HS | cnki:ISSN:1004-745X.0. | clinical manifestations | mecha | N/A | 50 | 212 | 30.9 | rectal | 48h | 6-72m |
| 2004 | 2004-08-022 | alone | nical | | | | | | | |
| Li HY | N/A | clinical manifestations | ileus | abdominal surgery | 160 | 160 | 28.5 | nasogastric tube/oral | N/A | N/A |
| 2006 | | alone | | | | | | | | |
| Li R | CNKI:ISSN:1006-978X. | diagnostic imaging + | mecha | abdominal surgery | 24 | 56 | 41 | rectal | 15d | N/A |
| 2007 | 0.2007-01-010 | clinical manifestations | nical | | | | | | | |
| Li ZY | cnki:ISSN:1000-7369.0. | clinical manifestations | ileus | abdominal surgery | 15 | 50 | 48.7 | rectal | 72h | N/A |
| 2006 | 2006-01-038 | alone | | | | | | | | |
| Liang QF | cnki:ISSN:0256-7415.0. | diagnostic imaging + | mecha | abdominal surgery | 29 | 51 | 36.9 | rectal | 3d | N/A |
| 2004 | 2004-07-025 | clinical manifestations | nical | | | | | | | |
| Liang WH | CNKI:SUN:YYXK.0.20 | diagnostic imaging + | ileus | abdominal surgery | 35 | 68 | 41.85 | nasogastric tube/oral | 7d | N/A |
| 2010 | 10-20-028 | clinical manifestations | | | | | | | | |
| Liao DX | CNKI:SUN:XLCL.0.200 | diagnostic imaging + | mecha | abdominal surgery | 52 | 136 | N/A | nasogastric tube/oral | N/A | 1m |
| 2009 | 9-28-022 | clinical manifestations | nical | | | | | | | |
| Liao ZY | cnki:ISSN:1008-2409.0. | clinical manifestations | ileus | abdominal surgery | 28 | 80 | 37.5 | rectal | 99h | N/A |
| 2006 | 2006-04-043 | alone | | | | | | | | |
| Liu JS | N/A | clinical manifestations | mecha | abdominal surgery | 19 | 36 | 32.7 | (nasogastric tube/oral) and rectal | N/A | N/A |
| 1996 | | alone | nical | | | | | | | |
| Liu P | CNKI:SUN:ZGSQ.0.20 | clinical manifestations | ileus | abdominal surgery | N/A | 207 | N/A | rectal | N/A | 0.5-1y |
| 2009 | 09-19-173 | alone | | | | | | | | |
| Liu Q | N/A | clinical manifestations | ileus | N/A | 33 | 60 | 53.5 | nasogastric tube/oral | N/A | N/A |
| 2009 | | alone | | | | | | | | |
| Liu XH | cnki:ISSN:1003-7705.0. | diagnostic imaging + | ileus | abdominal surgery | 24 | 50 | 50.7 | rectal | 35d | 114m |
| 2005 | 2005-01-009 | clinical manifestations | | | | | | | | |

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| | | | | | | | | | | |
|-------------------------------|---------------------------------------|---|----------------|--|-----|-----|------|---------------------------------------|-----|--------|
| Lu YH 2008 | CNKI:SUN:ZWYY.0.20 08-07-050 | diagnostic imaging + clinical manifestations | mecha nical | N/A | 44 | 96 | 50 | nasogastric tube/oral | 7d | N/A |
| Luo M 2005 | cnki:ISSN:1007-6948.0. 2005-01-011 | clinical manifestations alone | ileus | abdominal surgery | 41 | 97 | 40.4 | rectal | N/A | 1-1.5y |
| Ma ZJ 2005 | cnki:ISSN:0256-7415.0. 2005-07-015 | clinical manifestations alone | ileus | fracture thoracic vertebrae or lumbar vertebrae | 20 | 60 | N/A | nasogastric tube/oral | 6d | N/A |
| Peng T 2010 | CNKI:SUN:YXSS.0.201 0-09-244 | diagnostic imaging + clinical manifestations | mecha nical | abdominal surgery | 35 | 116 | 42.4 | nasogastric tube/oral | 7d | N/A |
| Qiu JF 2009 | CNKI:SUN:XXYY.0.20 09-06-049 | clinical manifestations alone | ileus | abdominal surgery | 21 | 60 | 51.7 | nasogastric tube/oral | N/A | N/A |
| Shen JQ 2005 | cnki:ISSN:1005-4561.0. 2005-10-005 | diagnostic imaging + clinical manifestations | ileus | abdominal surgery, gastrointestinal neoplasm | 20 | 56 | 34.8 | (nasogastric tube/oral) and rectal | 18d | N/A |
| Su SH 2008 | CNKI:SUN:QKYX.0.20 08-22-032 | diagnostic imaging + clinical manifestations | ileus | N/A | 6 | 15 | N/A | nasogastric tube/oral | 7d | N/A |
| Sui J 2010 | CNKI:SUN:SYYZ.0.20 10-12-078 | diagnostic imaging + clinical manifestations | mecha nical | N/A | 43 | 108 | 51.2 | (nasogastric tube/oral) and rectal | 7d | N/A |
| Sun JJ 2006 | cnki:ISSN:1000-7369.0. 2006-01-037 | clinical manifestations alone | ileus | abdominal surgery | 155 | 302 | 67.8 | nasogastric tube/oral | N/A | N/A |
| Tang ZA 2008 | CNKI:SUN:SYLC.0.200 8-11-065 | diagnostic imaging + clinical manifestations | mecha nical | abdominal surgery | 21 | 60 | 41.5 | (nasogastric tube/oral) and rectal | 10d | N/A |
| Tao YJ 2008 | CNKI:SUN:XDJH.0.200 8-21-058 | diagnostic imaging + clinical manifestations | mecha nical | abdominal surgery | 64 | 170 | 46.1 | nasogastric tube/oral | 4d | N/A |
| Tong FG 2006 | N/A | clinical manifestations alone | mecha nical | N/A | 22 | 64 | N/A | nasogastric tube/oral | 3d | N/A |
| Wang CG 2010 | CNKI:SUN:JYGZ.0.201 0-02-032 | diagnostic imaging + clinical manifestations | ileus | abdominal surgery | 15 | 38 | 31.7 | (nasogastric tube/oral) and rectal | 10d | N/A |
| Wang CH 2009 | CNKI:SUN:HNZY.0.20 09-06-017 | clinical manifestations alone | ileus | abdominal surgery | 150 | 150 | 44.8 | nasogastric tube/oral | 2d | N/A |
| Wang P 2007 | CNKI:ISSN:1004-0501. 0.2007-05-042 | diagnostic imaging + clinical manifestations | mecha nical | tuberculous peritonitis | 36 | 65 | 38.6 | rectal | 72h | N/A |
| Wang W | cnki:ISSN:1671-4040.0. | diagnostic imaging + | mecha | abdominal surgery | 56 | 162 | N/A | nasogastric tube/oral | N/A | N/A |

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| | | | | | | | | | | |
|-----------------|------------------------|-------------------------|-------|---------------------|----|-----|------|------------------------------------|------|-----|
| 2004 | 2004-03-014 | clinical manifestations | nical | | | | | | | |
| Wang YF | CNKI:SUN:PTGZ.0.200 | diagnostic imaging + | mecha | abdominal surgery | 70 | 127 | 49 | nasogastric tube/oral | N/A | N/A |
| 2009 | 9-05-009 | clinical manifestations | nical | | | | | | | |
| Wen JY | CNKI:SUN:ZWYY.0.20 | diagnostic imaging + | ileus | abdominal surgery | 13 | 32 | 40.2 | rectal | N/A | N/A |
| 2008 | 08-05-038 | clinical manifestations | | | | | | | | |
| Wu CT | cnki:ISSN:1001-5426.0. | diagnostic imaging + | mecha | abdominal surgery | 58 | 248 | 40.9 | nasogastric tube/oral | 24h | N/A |
| 2003 | 2003-02-011 | clinical manifestations | nical | | | | | | | |
| Wu DH | CNKI:SUN:FJZY.0.200 | clinical manifestations | mecha | abdominal surgery | 20 | 52 | 51.5 | rectal | 7d | N/A |
| 2009 | 9-06-030 | alone | nical | | | | | | | |
| Xie ZC | CNKI:SUN:YLQY.0.20 | diagnostic imaging + | mecha | abdominal surgery | 59 | 125 | 37.5 | rectal | N/A | N/A |
| 2008 | 08-06-061 | clinical manifestations | nical | | | | | | | |
| Xu HY | CNKI:SUN:MZMJ.0.20 | diagnostic imaging + | ileus | abdominal surgery | 25 | 80 | 63.9 | nasogastric tube/oral | 10d | N/A |
| 2009 | 09-20-045 | clinical manifestations | | | | | | | | |
| Yang SZ | CNKI:SUN:JLYX.0.201 | clinical manifestations | ileus | abdominal surgery | 14 | 42 | 53.6 | (nasogastric tube/oral) and rectal | N/A | N/A |
| 2010 | 0-31-027 | alone | | | | | | | | |
| Ye B | N/A | diagnostic imaging + | mecha | abdominal surgery | 43 | 70 | N/A | (nasogastric tube/oral) and rectal | 5d | N/A |
| 2008 | | clinical manifestations | nical | | | | | | | |
| You L | CNKI:SUN:SJZX.0.200 | clinical manifestations | mecha | phytobezoar induced | 35 | 96 | 37.3 | nasogastric tube/oral | 3d | N/A |
| 2008 | 8-04-025 | alone | nical | obstruction | | | | | | |
| Zhang Y | CNKI:ISSN:0256-7415. | diagnostic imaging + | mecha | abdominal surgery | 41 | 97 | 38.8 | (nasogastric tube/oral) and rectal | 5d | N/A |
| 2007 | 0.2007-01-006 | clinical manifestations | nical | | | | | | | |
| Zhao Y | cnki:ISSN:0256-7415.0. | diagnostic imaging + | mecha | abdominal surgery | 44 | 117 | 43.9 | (nasogastric tube/oral) and rectal | 3-5d | N/A |
| 2006 | 2006-03-029 | clinical manifestations | nical | | | | | | | |
| Zhao YL | N/A | clinical manifestations | ileus | abdominal surgery | 82 | 162 | 46.1 | nasogastric tube/oral | N/A | N/A |
| 2006 | | alone | | | | | | | | |
| Zheng HL | CNKI:SUN:GDYY.0.20 | diagnostic imaging + | mecha | abdominal surgery | 40 | 100 | 46.5 | (nasogastric tube/oral) and rectal | 72h | N/A |
| 2010 | 10-04-071 | clinical manifestations | nical | | | | | | | |
| Zhou SY | CNKI:SUN:GYZX.0.20 | diagnostic imaging + | mecha | abdominal surgery | 40 | 86 | 44.5 | (nasogastric tube/oral) and rectal | 24h | N/A |
| 2009 | 09-04-022 | clinical manifestations | nical | | | | | | | |
| Zhou YJ | cnki:ISSN:1004-745X.0. | diagnostic imaging + | mecha | abdominal surgery | 16 | 78 | 45.8 | (nasogastric tube/oral) and rectal | N/A | N/A |
| 2001 | 2001-06-016 | clinical manifestations | nical | | | | | | | |

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Supplementary Table 2: Characteristics of the included RCTs (part B)

| Trials | Interventions (experimental group) | Interventions (control group) | Outcomes |
|----------------------|---|---|---|
| Ao XR 2007 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, laxatives (liquid paraffin), soapsuds enema, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, laxatives (liquid paraffin), soapsuds enema | improvement of clinical/imaging manifestations |
| Cao SB 2008 | bowel rest, intubation and decompression, intravenous fluid resuscitation, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation | improvement of clinical/imaging manifestations |
| Chen CQ 2002# | 1) DCQD <i>jiajian</i> 2) cisapride 3*10mg/d, DCQD <i>jiajian</i> | cisapride 3*10mg/d | time to first stool, length of hospital stay |
| Chen H 2009 | bowel rest, intubation and decompression, intravenous fluid resuscitation, DCQD <i>jiajian</i> 50mL/6h | bowel rest, intubation and decompression, intravenous fluid resuscitation antibiotics | time to first flatus, time to clinical/imaging manifestations improved, time to extubation, length of hospital stay |
| Chen ZJ 2004 | bowel rest, decompression, antibiotics, intravenous fluid resuscitation, DCQD 200ml/12h | bowel rest, decompression, antibiotics, intravenous fluid resuscitation | time to first stool, improvement of clinical manifestations |
| Dong ZC 2008 | bowel rest, decompression, intravenous fluid resuscitation, DCQD 175ml/12h, antibiotics | bowel rest, decompression, intravenous fluid resuscitation, soapsuds enema | improvement of clinical/imaging manifestations |
| Dou WH 2009 | bowel rest, decompression, antacid, intravenous fluid resuscitation, antibiotics, DCQD 200ml/24h | bowel rest, decompression, antacid, intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| Fan Y 2007 | DCQD 200ml/24h | cisapride 3*5mg/d | time to first bowel movement, improvement of clinical manifestations |
| Fang HL 2008 | bowel rest, decompression, intravenous fluid resuscitation, antibiotics, DCQD 200-300ml/24h | bowel rest, decompression, intravenous fluid resuscitation, antibiotics | time to first stool, improvement of clinical/imaging manifestations |
| Fu HB 2008 | bowel rest, decompression, intravenous fluid resuscitation, antibiotics, DCQD 200ml/24h | bowel rest, decompression, intravenous fluid resuscitation, antibiotics | time to first stool, improvement of clinical/imaging manifestations |
| Gao JC 2005 | decompression, intravenous fluid resuscitation, antibiotics, DCQD | decompression, intravenous fluid resuscitation, antibiotics | time to first flatus, improvement of clinical manifestations |
| Gao ZJ 2010 | bowel rest, intubation and decompression, intravenous fluid resuscitation, total parenteral nutrition, glucocorticoids, antibiotics, DCQD <i>jiajian</i> 100ml/12h, metoclopramide 10mg | bowel rest, intubation and decompression, intravenous fluid resuscitation, total parenteral nutrition, glucocorticoids, antibiotics | improvement of clinical/imaging manifestations, length of hospital stay |
| He GM 2009 | bowel rest, intubation and decompression, intravenous fluid resuscitation, total parenteral nutrition, glucocorticoids, antibiotics, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, total parenteral nutrition, | improvement of clinical/imaging manifestations, length of hospital stay |

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| | | | |
|----------------------|---|--|--|
| | 200ml/24h | glucocorticoids, antibiotics | |
| Hu ZG 2008 | bowel rest, intubation and decompression, intravenous fluid resuscitation, total parenteral nutrition, coloclisis with physiological saline, DCQT <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, total parenteral nutrition, coloclisis with physiological saline | improvement of clinical/imaging manifestations |
| Jiang CL 2008 | bowel rest, intubation and decompression, intravenous fluid resuscitation, total parenteral nutrition, antibiotics, coloclisis with 200ml DCQT <i>jiajian</i> (twice/day) | bowel rest, intubation and decompression, intravenous fluid resuscitation, total parenteral nutrition, antibiotics, coloclisis with 200ml physiologic saline (twice/day) | improvement of clinical/imaging manifestations |
| Jiang K 2009 | bowel rest, intubation and decompression, intravenous fluid resuscitation, somatostatin, histamine 2 blocking pharmacon, glucocorticoids, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, somatostatin, histamine 2 blocking pharmacon, glucocorticoids | improvement of clinical/imaging manifestations |
| Li H 2010 | bowel rest, intubation and decompression, intravenous fluid resuscitation, proton pump inhibitor, glucocorticoids, antibiotics, diuretic, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, proton pump inhibitor, glucocorticoids, antibiotics, diuretic | improvement of clinical/imaging manifestations, time to first flatus, time to first bowel movement, time to first stool, the duration of treatment |
| Li HS 2004 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> 100ml(2 times/day), | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | time to first stool, improvement of clinical manifestations |
| Li HY 2006 | DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation | time to first flatus |
| Li R 2007 | bowel rest, intubation and decompression, intravenous fluid resuscitation, somatostatin, histamine 2 blocking pharmacon, antibiotics, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, somatostatin, histamine 2 blocking pharmacon, antibiotics | improvement of clinical/imaging manifestations, length of hospital stay |
| Li ZY 2006 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD 200ml (twice/day) | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | time to first flatus, time to first stool, the gastrin level change, the vascular intestinal peptide(VIP) level |
| Liang QF 2004 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> 200ml (twice/day) | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| Liang WH 2010 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, glucocorticoids, somatostatin, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, glucocorticoids, somatostatin | time to first flatus, time to first stool, time to clinical/imaging manifestations improved, time to imaging improvement |
| Liao DX 2009 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, somatostatin, acupuncture moxibustion, DCQD <i>jiajian</i> , change position continuously | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, somatostatin, change position continuously | improvement of clinical/imaging manifestations |
| Liao ZY 2006 | intubation and decompression, intravenous fluid resuscitation, antibiotics, | intubation and decompression, intravenous fluid | improvement of clinical manifestations, time to first |

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| | | | |
|---------------------|--|---|---|
| | DCQD | resuscitation, antibiotics, coloclisis with glycerol | flatus, time to first stool, time to clinical manifestations improved |
| Liu JS 1996 | intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD | intubation and decompression, intravenous fluid resuscitation, antibiotics | time to first flatus, time to first stool, time to recovery of body temperature, length of hospital stay, complications |
| Liu P 2009 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, vitamin B1, DCQD | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, vitamin B1 | improvement of clinical manifestations |
| Liu Q 2009 | antibiotics, DCQD | intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical manifestations |
| Liu XH 2005 | bowel rest, intravenous fluid resuscitation, intubation and decompression, antibiotics, glucocorticoids, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, laxatives (glycerol, liquid paraffin or castor oil) | improvement of clinical/imaging manifestations |
| Lu YH 2008 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| Luo M 2005 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | first bowel movement, time to first flatus, time to first stool |
| Ma ZJ 2005 | intravenous fluid resuscitation, DCQD <i>jiajian</i> | intubation and decompression, laxative(glycerine enema or folium sennae), intravenous fluid resuscitation | improvement of clinical manifestations |
| Peng T 2010 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, somatostatin, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, somatostatin | response rate, time to clinical/imaging manifestations improved |
| Qiu JF 2009 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> 50ml/12h | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, physiological saline 50ml/12h | time to first stool |
| Shen JQ 2005 | intubation and decompression, intravenous fluid resuscitation, antibiotics, glucocorticoids, omatostatin, CQD <i>jiajian</i> 200ml/d | intubation and decompression, intravenous fluid resuscitation, antibiotics, glucocorticoids, somatostatin | improvement of clinical/imaging manifestations, time to relief of symptome |
| Su SH 2008 | DCQD <i>jiajian</i> (100ml/12h) | primperan 2*10mg/d and mosapride 3*5mg/d | improvement of clinical/imaging manifestations, time to bowel open |
| Sui J 2010 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, somatostatin, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, somatostatin | improvement of clinical/imaging manifestations |
| Sun JJ 2006 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> 100ml/12h | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical manifestations, incidence of complications |
| Tang ZA 2008 | bowel rest, intubation and decompression, intravenous fluid resuscitation, | bowel rest, intubation and decompression, intravenous | improvement of clinical manifestations |

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| | | | |
|---------------------|---|--|---|
| | antibiotics, DCQD <i>jiajian</i> | fluid resuscitation, antibiotics | |
| Tao YJ 2008 | bowel rest, intubation and decompression, intravenous fluid resuscitation, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation | improvement of clinical/imaging manifestations |
| Tong FG 2006 | bowel rest, intubation and decompression, intravenous fluid resuscitation, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, liquid paraffin | improvement of clinical manifestations |
| Wang CG 2010 | analgesia, somatostatin, proton pump inhibitors, antibiotics, glucocorticoids (dexamethasone), DCQD <i>jiajian</i> | analgesia, somatostatin, proton pump inhibitors, antibiotics, glucocorticoids (dexamethasone) | improvement of clinical/imaging manifestations |
| Wang CH 2009 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, somatostatin, proton pump inhibitors, DCQD <i>jiajian</i> 100ml/12h | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, somatostatin, proton pump inhibitors | improvement of clinical manifestations |
| Wang P 2007 | anti-tuberculosis, bowel rest, intubation and decompression, intravenous fluid resuscitation, DCQD <i>jiajian</i> | anti-tuberculosis, bowel rest, intubation and decompression, intravenous fluid resuscitation | improvement of clinical/imaging manifestations |
| Wang W 2004 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| Wang YF 2009 | bowel rest, intubation and decompression, intravenous fluid resuscitation, sandostatin, omeprazole, DCQD | bowel rest, intubation and decompression, intravenous fluid resuscitation, sandostatin, omeprazole | improvement of clinical/imaging manifestations, time to first flatus/stool, time to relief of abdominal pain, time to first bowel movement, time to improvement of imaging manifestations |
| Wen JY 2008 | intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> | intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| Wu CT 2003 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | time to first stool, improvement of clinical/imaging manifestations |
| Wu DH 2009 | intubation and decompression, intravenous fluid resuscitation, antibiotics, analgesia, DCQD | intubation and decompression, intravenous fluid resuscitation, antibiotics, analgesia | improvement of clinical manifestations |
| Xie ZC 2008 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| Xu HY 2009 | bowel rest, intubation and decompression, intravenous fluid resuscitation, octreotide, ranitidine, dexamethasone, diuretics, antibiotics, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, octreotide, ranitidine, dexamethasone, diuretics, antibiotics | time to first flatus, time to first bowel movement, time to relief of symptom, improvement of clinical/imaging manifestations |
| Yang SZ 2010 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | time to first flatus |

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| | | | |
|----------------------|---|---|---|
| Ye B 2008 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| You L 2008 | bowel rest, intubation and decompression, intravenous fluid resuscitation, soapsuds enema, antibiotics, DCQD <i>jiajian</i> , electro acupuncture | bowel rest, intubation and decompression, intravenous fluid resuscitation, soapsuds enema, antibiotics | length of hospital stay, improvement of clinical manifestations |
| Zhang Y 2007 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| Zhao Y 2006 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, CQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| Zhao YL 2006 | DCQD <i>jiajian</i> | intubation and decompression, intravenous fluid resuscitation, antibiotics | time to first flatus, time to first stool |
| Zheng HL 2010 | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| Zhou SY 2009 | bowel rest, intubation and decompression, laxatives (liquid paraffin), intravenous fluid resuscitation, antibiotics, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, laxatives (liquid paraffin), intravenous fluid resuscitation, antibiotics | improvement of clinical/imaging manifestations |
| Zhou YJ 2001 | bowel rest, intubation and decompression, intravenous fluid resuscitation, DCQD <i>jiajian</i> | bowel rest, intubation and decompression, intravenous fluid resuscitation | improvement of clinical/imaging manifestations |

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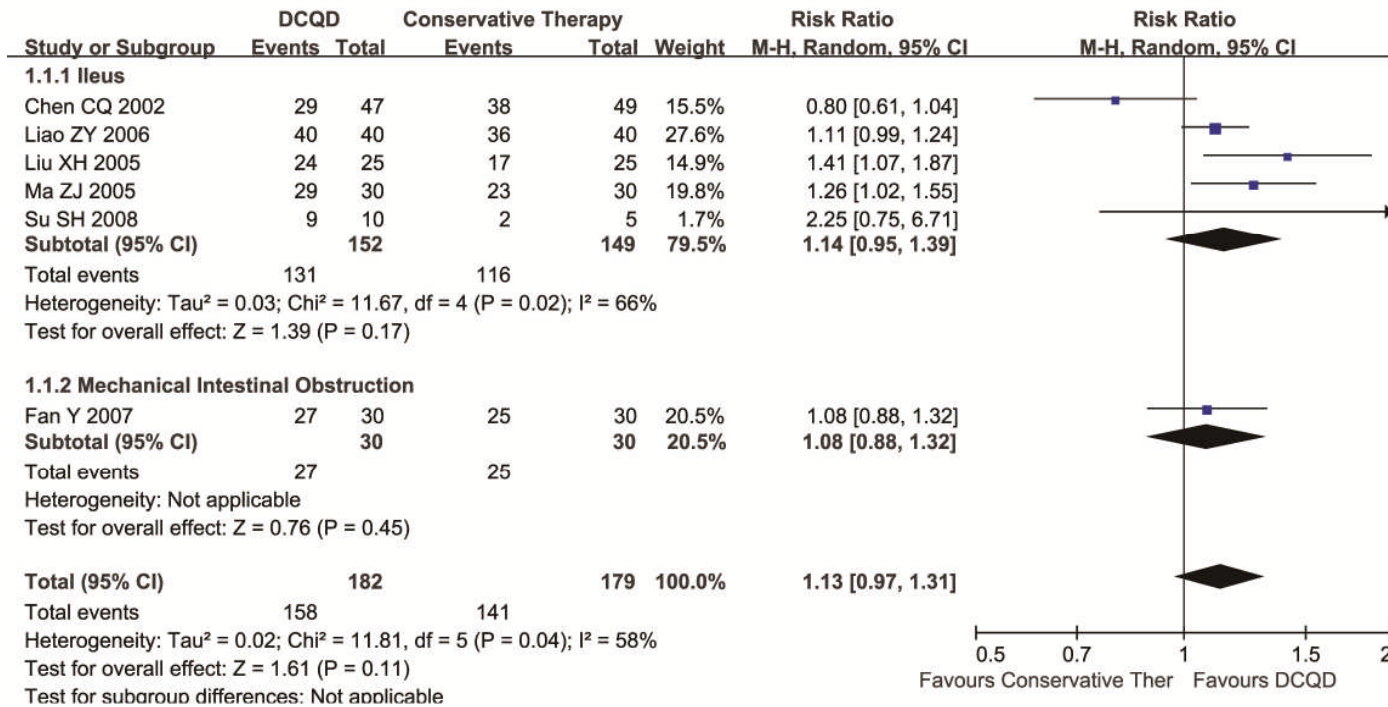


Figure 2: Effect of DCQD compared with conservative therapy in treatment of intestinal obstruction

DCQD, Da-Cheng-Qi decoction; 95% CI, 95% confidence interval

Note that Risk Ratio < 1 means numerically lower response rate than control group and RR > 1 numerically higher response rate than control group. 95% CI doesn't include the number 1 means statistical difference between the 2 groups.

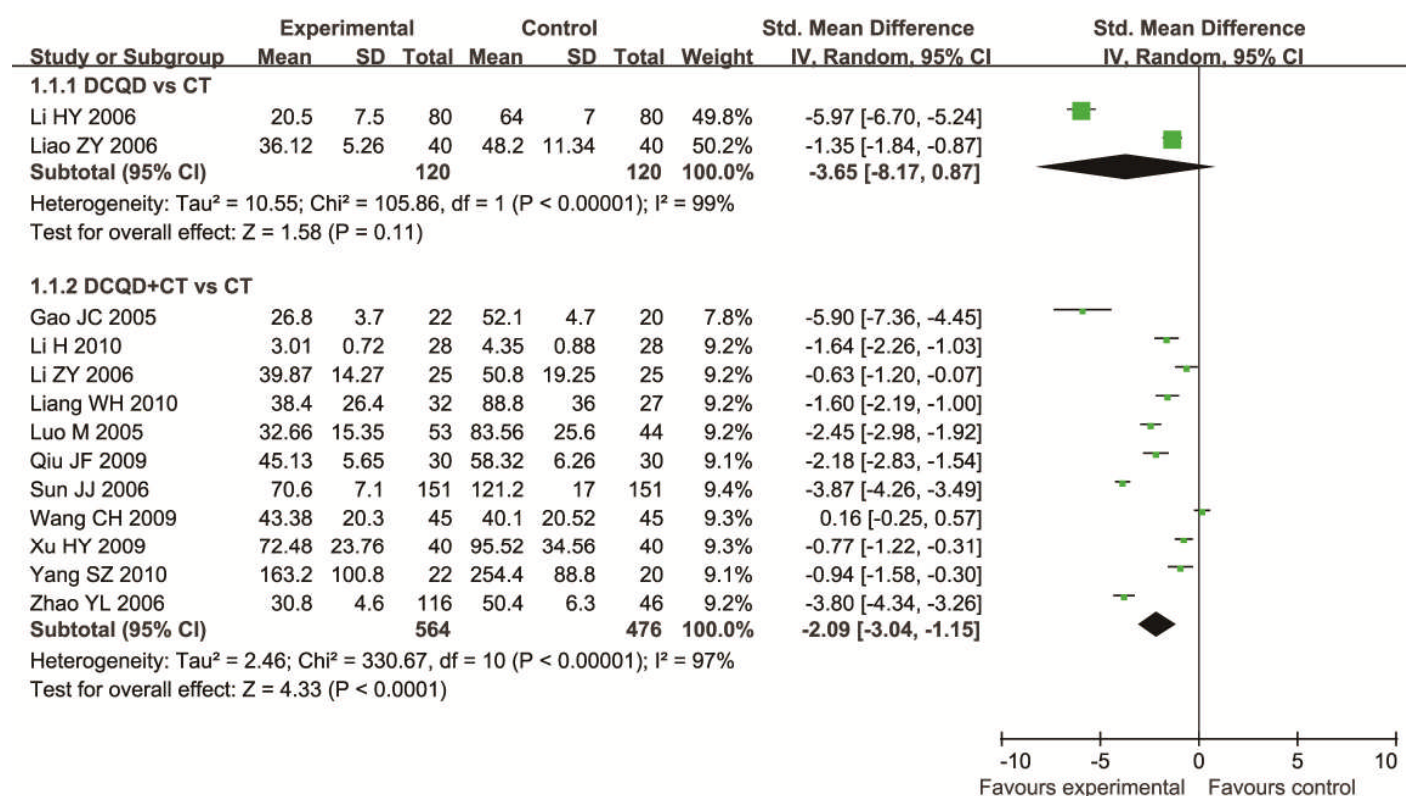


Figure 3: Forest plot of the time to first flatus

SMD, standardised mean difference; 95% CI, 95% confidence interval

Note that $SMD < 0$ means numerically time to first flatus in experiment group is shorter than control group and $SMD > 0$ numerically time to first flatus in experimental group is longer than control group. 95% CI doesn't include the number 0 means statistical difference between the 2 groups

Response to therapy in patients with mechanical intestinal obstruction

The 33 RCTs studying mechanical intestinal obstruction reported dichotomous data of 3,748 patients. Mechanical intestinal obstruction of 2,845 patients was caused by postoperative adhesion. Overall, 170 (8.4%) of 2,035 patients assigned to DCQD plus conservative therapy failed to respond to therapy compared with 498 (29.1%) of 1,713 patients allocated to conservative therapy (RR of respond = 1.26; 95% CI 1.21 to 1.31 which favoured DCQD plus conservative therapy) (Fig 4), with no significant heterogeneity between studies ($I^2=38\%$) and an NNT of 5.3 (95% CI 4.5 to 5.9). There was no evidence of funnel plot asymmetry (Begg's test, $p=0.05$).

Given the borderline heterogeneity observed when results of individual RCTs were combined, we conducted pre-specified sensitivity analyses (Table 2). The RR of respond was relatively stable in all these analyses. Heterogeneity between trials was lower when only the 22 studies that administrate DCQD via oral or when only the 12 studies that via rectal were included in the analysis. In addition, the results of sensitivity analyses showed that DCQD administration via rectal seems to be more effective (NNT = 4.2 95% CI 3.6 to 5.3). Treatment effect remained similar when only the 23 trials at moderate risk of bias were considered.

Discussion

This systematic review and meta-analysis has demonstrated that DCQD plus conservative therapy were more effective than conservative therapy alone for the treatment of intestinal obstruction, these beneficial effects appeared to exist for both ileus and mechanical intestinal obstruction. In addition, DCQD administration via rectal seems to be more effective. The RR of respond was relatively stable in all the sensitivity analyses. There was no statistical difference when we compared DCQD mono-therapy with conservative therapy alone. Although DCQD appear to be more effective than conservative therapy when the only two studies using clinical manifestations and imaging test improvement to define

response to treatment, considering there are only 60 subjects left in these two trials, we could draw no conclusion safely. For the continuous data of the time to first flatus, we found that DCQD plus conservative therapy could significantly shorten the duration of postoperative ileus in patients undergoing abdominal surgery.

Pharmacological studies and animal experiments have proved that effective components in DCQD could prevent intestinal adhesion by reducing the concentration of fibrinogen and raising that of fibrin degrading products in the intro-abdominal exudates after major abdominal surgery (Wang et al., 2004), and rhubarb in *Radix et Rhizoma Rhei* effects on colon (Jin et al, 2013) and increases the tension of it. Emodin can enhance the function of small intestinal peristalsis by mechanisms of promoting secretion of motilin, lowering the content of somatostatin and inhibiting sodium-potassium-exchanging ATPase activity of small intestinal mucosa (Zhang et al., 2005). Results of our research corroborated these previous pharmacological studies and animal experiments from another angle.

This systematic review has several strengths. To our knowledge, this is the first meta-analysis that focuses on the efficacy and safety of DCQD in the treatment of intestinal obstruction. The systematic review includes 60 RCTs with 6,095 patients, which makes it a powerful systematic review to analyze the efficacy and safety of DCQD. The study population well represented the general intestinal obstruction population in terms of age and pathogenesis. The success rate of conservative therapy alone was near to the previous study reported (Tanaka et al., 2008). We were also rigorous in describing our search strategy, eligibility criteria, and data extraction processes in detail. We conducted subgroup analysis to maintain clinical homogeneity in the patients, and sensitivity analyses according to risk of bias of included trials, route of administration, definition of response to therapy and aetiology to assess whether any of these trial characteristics affected overall efficacy. We used an intention-to-treat analysis, where all drop-outs assumed to be treatment failures, and pooled data with a random effects model, in order to reduce the likelihood that any beneficial effect of DCQD in intestinal obstruction has been overestimated.

Limitations of the present study, as with any systematic review and meta-analysis, arise from the quality and reporting of the RCTs included. Methodologies of RCTs conducted in mainland China where various and some of the included RCTs did not report their results according to the CONSORT checklist strictly. Blinding and allocation concealment were not reported in these RCTs, which means potential risk of bias. (Wood et al., 2008; He et al., 2011). There was borderline heterogeneity when dichotomous data were pooled, but our sensitivity analyses revealed plausible explanations for this. As for the significant heterogeneity when continuous data were pooled, the potential reasons may be the trials were carried out by surgeons with different technical levels, and clinical background was various among the subjects included, thus clinical heterogeneity inevitably existed. To perform subgroup analysis according to the type of surgical approach and the type of anaesthesia was meaningful, but we could not do this because little trials reported results separately by detailed clinical backgrounds. However, this problem did not prevent us from making a positive conclusion as other systematic reviews did.(Ford et al., 2009; Ford et al., 2011). Total adverse events data for DCQD via oral or rectal were sparse, this, however, may because the side-effects of short-term use of DCQD were light (Zhang et al., 2008;

Maxion-Bergemann et al., 2006; Kaszkin-Bettag et al., 2008) and easily be overwhelmed by the primary diseases. Lack of long-term follow-up prevented us from analysing the recurrence rate of intestinal obstruction.(Fevang et al., 2004) As limitations stated here, future well designed; randomised; double-blind; multicentre; long-term follow-up studies are needed to investigate these unanswered questions.

In summary, current guidelines for the management of intestinal obstruction from national and international do not pay much attention to any kinds of complementary and alternative medicine,(Diaz et al., 2008; Catena et al., 2011) evidence from this systematic review and meta-analysis supports the use of DCQD plus conservative therapy, which may increase the success rate of conservative therapy significantly and shorten the duration of postoperative ileus in patients undergoing abdominal surgery.

Contributors: Ling Tang acts as guarantor for the validity of the study report. Study concept and design: TL, LCQ. Acquisition of data: YB, XFY. Data Check: SHJ. Analysis and interpretation of data: YB, SHJ. Draft of manuscript: XFY, SXY. Critical revision of the manuscript for important intellectual content: ZZ, SXY. Statistical analysis: YB, XFY, SHJ.

Conflict of interest: All the authors declared no potential conflict of interest.

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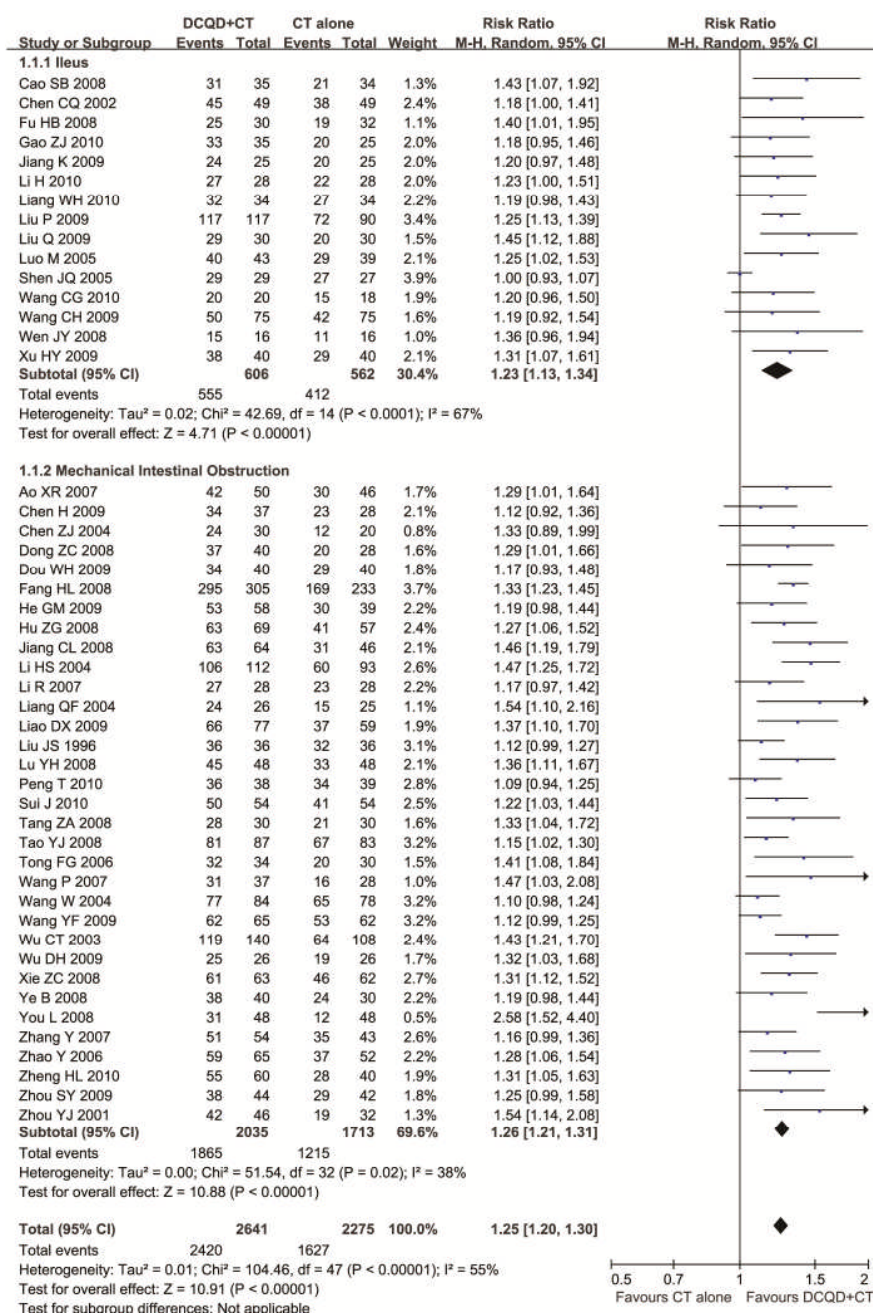


Figure 4: Effect of DCQD plus conservative therapy compared with conservative therapy in treatment of intestinal obstruction

CT, conservative therapy; DCQD, Da-Cheng-Qi decoction; 95% CI, 95% confidence interval

Note that $RR < 1$ means numerically lower response rate than control group and $RR > 1$ numerically higher response rate than control group. 95% CI doesn't include the number 1 means statistical difference between the 2 groups.

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