A Systematic Review of Chinese Medicinal Herbs for Acute Bronchitis

JIAFU WEI, M.Sc., JUAN NI, M.Sc., TAIXIANG WU, M.Sc., XIAOYAN CHEN, M.Sc.,
XIN DUAN, M.Sc., GUANJIAN LIU, M.Sc., JIEQI YIAO, M.Sc., QIN WANG, M.Sc.,
JIE ZHEN, M.Sc., and LIKUN ZHOU, M.Sc.

ABSTRACT

Objectives: To assess the effectiveness and safety of Chinese medicinal herbs for treating uncomplicated acute bronchitis.

Data sources: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), which includes the Cochrane Acute Respiratory Infections Group’s specialized register; The Chinese Cochrane Centre’s Controlled Trials Register; MEDLINE®; EMBASE; and the Chinese Biomedical Database (CBM).

Methods: We only included randomized controlled trials. At least two authors extracted data and assessed trial quality.

Main results: Four trials reported the time to improvement of cough, fever, and rales associated with bronchitis and showed that patients treated with Chinese herbs had a shorter duration of signs and symptoms. Two trials reported the proportion of patients with improved signs and symptoms at follow-up and showed that Chinese herbs were beneficial in terms of relief of signs and symptoms. Thirteen (13) trials analyzed the data on physician global assessment of improvement at follow-up. Nine (9) of 13 trials showed that Chinese herbs were superior to routine treatment and the other four trials showed a similar effect to routine treatment. In general, Chinese herbs appeared beneficial. Only one trial reported adverse effects during treatment.

Conclusions: There are insufficient quality data to recommend the routine use of Chinese herbs for acute bronchitis. The benefit found in this systematic review could be due to publication bias and study-design limitations of the individual studies. In addition, the safety of Chinese herbs is unknown due to the lack of toxicological evidence on these Chinese herbs, though adverse events are rarely reported.

BACKGROUND

Acute bronchitis is one of the most common diagnoses made by primary care physicians.1-3 This condition accounted for approximately 2.5 million visits to U.S. physicians in 1998.4 It consistently ranks as one of the top 10 diagnoses for which patients seek medical care, with cough being the most frequently mentioned symptom.4 During each episode, patients receive an average of two prescriptions and miss 2 to 3 days of work.5 Viruses are the most common cause of the bronchial inflammation associated with acute bronchitis in otherwise healthy adults. Only a small proportion of acute bronchitis infections are caused by non-viral agents, with the most common organism being Mycoplasma pneumoniae (M. pneumoniae).6-8 Study findings suggest that Chlamydia pneumoniae (C. pneumoniae) also may cause acute bronchitis.10,11 Antibiotics are the predominant therapy offered to patients with acute bronchitis.11 However, there is evidence...
for the effectiveness of antibiotics over placebo of modest benefit only. Symptomatic treatments have even less evidence, and include: antitussives for cough; expectorants for sputum too viscous to expectorate; bronchodilators for cough associated with any associated asthma; and antipyretic analgesics for fever.

In China, many physicians believe that herbs are effective for acute bronchitis. Some Chinese herbs have been demonstrated to be antiviral, antiasthmatic, antitussive, and fever relieving. For example, Radix scutellariae has antiphlogistic effects; Radix glycyrrhizae has expectorant effects; and Folium perillae has antitussive effects. Herbs for various symptoms or causes are combined in set quantities as a basic prescription to treat acute bronchitis.

Natural medicinal herbs are a potential drug resource. Therefore, a systematic review of the evidence as to whether or not these medicinal herbs are effective for acute bronchitis.

**METHODS**

Criteria for considering studies for this review

**Types of studies.** Randomised controlled trials (RCTs).

**Types of participants.** Trials which included patients of either gender or any age with a clinical syndrome of cough and productive sputum or a physician’s diagnosis of acute bronchitis were included. Trials which included patients with pre-existing chronic bronchitis (that is, acute exacerbation of chronic bronchitis) or other infectious diseases and fever-causing diseases were not included.

**Types of interventions.** Studies comparing any Chinese herbal combination to placebo, antibiotics, or other routine care were acceptable.

**Types of outcome measures.** We included outcomes of clinical importance. These outcomes were as follows:

1. Time to resolution of cough, sputum production, and activity limitations
2. Proportions of patients with cough, night cough, productive cough, activity limitations, or abnormal lung examination at a designated follow-up visit
3. Global assessment of improvement by clinicians at follow-up
4. Adverse effects

**Data sources**

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 1, 2005), which includes the Cochrane Acute Respiratory Infections Group’s specialised register; The Chinese Cochrane Centre’s Controlled Trials Register (up to December 2004); MEDLINE® (1966 to March Week 1, 2005); EMBASE (1988 to December 2004); and the Chinese Biomedical Database (CBM) (1980 to December 2004) were searched.

The search strategy defined by the Cochrane Collaboration and detailed in Appendix 5c of the Cochrane Reviewers’ Handbook (Edition 4.2.2). The search terms were bronchitis and Chinese herbs.

We also searched databases of ongoing trials: Current Controlled Trials (www.controlled-trials.com) and the National Research Register (www.update-software.com/National/nrr-frame.html). We attempted to identify additional studies by searching the reference lists of relevant trials, reviews, conference proceedings, and journals. In particular, with respect to journals, we searched those not indexed in the electronic databases.

**Methods of the review**

**Trials selection.** Titles and abstracts were reviewed from articles found in the searches. Those that appeared eligible were retrieved as full text articles. The inclusion criteria were applied by two authors independently. Disagreements were resolved by consensus, and the authors of the trials were contacted for more details when needed.

**Quality assessment of trials.** Wei and Wu assessed methodological quality of each trial in terms of generation of allocation sequence, allocation concealment, blinding, and loss to follow-up. For each trial, we classed each quality component as “adequate,” “inadequate,” “unclear,” or “not used,” according to Schulz and Jadad and the Cochrane Reviewers’ Handbook 4.2.2. After including all eligible studies in the primary analysis, we intended to conduct sensitivity analyses for each of the quality factors using the subgroups adequate, inadequate, or unclear.

**Data extraction.** Wei and Wu independently extracted data using a piloted data extraction form. We extracted data on study characteristics including methods, participants, interventions, and outcomes. We resolved any disagreements by referring to the trial report and through discussion. If data from the trial reports were insufficient or missing, we contacted the authors for additional information. If the authors could not be contacted, we allocated the study to the category “Studies awaiting assessment.” Where possible, we extracted data to allow an intention-to-treat analysis (the analysis should include all the participants in the groups to which they were originally randomly assigned). If the number randomised and the numbers analysed were inconsistent, we calculated the percentage lost to follow-up and reported this information separately. For binary outcomes, we recorded the number of participants experiencing the event in each group of the trial.
tiniuous outcomes, for each group we extracted the arithmetic means and standard deviations.

Extraction was undertaken by one reviewer and checked by a second. Data entry into RevMan (free software downloadable from www.cc_ims.net/RevMan.download.htm) was double-checked.

Data analysis. We had planned to include data with the same medicinal herbs in a meta-analysis. However, as none of the trials were similar in participants and/or interventions, we provided a summary of each trial.

If, in the future, enough suitable trials for meta-analysis become available, we will use the following approach.

The data will be dichotomised and expressed as relative ratio (RR).

Overall results will be calculated based on the random-effects model. Heterogeneity will be tested for using the Chi square statistic with significance being set at a $p$-value less than 0.1 and I square more than 50%. Possible sources of heterogeneity will be assessed by sensitivity and subgroup analyses. Publication bias will be tested by using the funnel plot or other corrective analytical method, depending on the number of clinical trials included in the systematic review.

Description of studies

We found 30 clinical RCTs on the use of Chinese medicinal herbs for acute bronchitis, and 14 of these were included in the review (Table 1). In 12 of the excluded studies Chinese medicinal herbs were administered in both the intervention and control groups, which did not meet the intervention criteria. In the other four trials the methods of randomisation allocation were inadequate.

Designs of included studies. Details of the included studies are shown in Table 1. All included studies were described as randomised controlled parallel trials. All studies mentioned “random allocation” but without an explanation of the randomisation method. None of the studies mentioned “blinding” or “allocation concealment.” The duration of trials ranged from 2 to 14 days. All of the trials were conducted in China.

Participants of included studies. The number of participants in the studies ranged from 82 to 456, with a total of 2771. All the patients were diagnosed with acute bronchitis by physicians. Three trials19–21 focused on adults aged over 16 years old, nine trials22,30 were limited to children aged below 14 years old, and the other two trials31,32 had no limitation on age.

In eight studies,19,20,26–30 the duration of illness was not expressed clearly; and in six trials it ranged from 1 to 60 days. The baseline data were stated in all trials and the comparability was analysed.

Interventions. Twelve Chinese herbal preparations used for acute bronchitis were analysed. They were as follows: Tan Re Qing injection,19 Dai Zhe Zhi Sou San,31 E Shu You,26 Zeng Xiao Zhi Ke He Ji,20 Shi Wei Long Dan Hua Ke Li,22,23,28 Shuang Huang Lian,21 Xiao Er Xiao Ji Zhi Ke Kou Fu Ye,25 “atomization of Yu Xing Cao injection”,27 Yu Xing Cao injection,30 Jia Wei Zhi Sou San,30 Zhi Sou San,32 Zi Yi San Ye Shuang Hua Tang.24

In seven trials21,22,26–30 antibiotics were used in both the intervention and control groups. In three of these trials21,26,30 antibiotics, antitussives, expectorants, and bronchodilators were used in both intervention and control groups.

In three trials25,31,32 Chinese herbal preparations were used in the intervention group and antibiotics plus expectorants and antitussives were used in the control group.

In four trials19,20,23,24 Chinese herbal preparations were used in the intervention group and antibiotics used in the control group.

Outcome measures. The majority of trials used the physician’s global assessment of improvement at follow-up; the timing of assessment varied from trial to trial. Two trials119,22 evaluated the proportion of patients with a variety of improved signs and symptoms. Three trials25,27,28 analysed the time to resolution of cough, rales, and fever. One trial25 assessed the time to resolution of wheezing. One trial19 evaluated the time to relief of cough and fever.

Methodological quality of included studies. All of the trials were randomised controlled trials comparing a preparation of Chinese medicinal herbs with “standard treatment.” Seven of the trials used antibiotics in both groups. All of the studies mentioned random allocation but none of the trials clearly stated the randomisation method. None of the articles mentioned allocation concealment.

None of the studies mentioned either double- or single-blinding. Most preparations of Chinese medicinal herbs differ from Western medicine in terms of smell, taste, type, and colour. It was difficult, therefore, to use double blinding when administering the interventions. However, double-blinding can be used for some dosage forms such as an injection or capsule.

None of the trials reported withdrawals or loss to follow-up.

None of the trials reported the methods to ensure compliance.

The similarity of comparison groups at baseline was reported in all trials based on age, gender, and disease duration at entry.

RESULTS

Time to improvement of symptoms and signs (Fig. 1)

1. Cough: Data from four trials showed that the duration of cough was shorter in the Chinese herbs group than in the control group.
<table>
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<th>Study ID</th>
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<td>An 2003</td>
<td>Parallel design. Randomisation procedure unclear. Blinding not used. Allocation concealment unclear.</td>
<td>68 adults (aged 19 to 60), diagnosed with acute bronchitis defined in The Golden Rule for Clinical Research of New Traditional Chinese Drugs (Zhongyao Xinyao Linchuanyangju Zhidao yuanze).</td>
<td>1. Intervention: “Tan Re Qing” injection (extract of baikal skullcap root, bear gall, horn of goat, honeysuckle flower, and weeping forsythia capsule) (20 mL qd for 10 days) 2. Control: levofloxacin (400 mg qd for 10 days)</td>
<td>Fever, cough, tongue picture, type of pulse, chest signs, hemogram and chest film scored with 0, 1, 2, and 3 before and after treatment for 7 days. Global assessment of improvement with total scores at follow-up on day 7, and graded with recovery (total score reduced by ( \geq 80% )) Marked effect: total score reduced by ( \geq 50% ) General effect: total score reduced by ( \geq 20% ) No effect: total score reduced by ( &lt; 20% ) Adverse effect: portion of fever, cough, and rhonchi relief Marked effect: all patients recovered within 3 days General effect: all patients experienced relief within 1 week Ineffective: no improvement over 1 week</td>
</tr>
<tr>
<td>Chen 2002</td>
<td>Parallel design. Randomisation procedure unclear. Blinding not used. Allocation concealment unclear.</td>
<td>141 in-patients manifested with cough, fever, rale, and rhonchi (duration: 3 to 10 d)</td>
<td>1. Intervention: antibiotics and “Shi Wei Long Dan Hua Ke Li” (components: gentian flower, savory rhododendron leaf, liquorice root, herba corydalis, rhizoma codonopsis convolvulacea, unibract fritillary bulb, crab shell, costustoot) 2. Control: antibiotics.</td>
<td>Marked improvement: all manifestations resolved within 7 days General improvement: all manifestations resolved, but relapsed once in a while during 14-day treatment Ineffective: no improvement with treatment of 14 days</td>
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<td>Qing 2002</td>
<td>Parallel design. Randomisation procedure unclear. Blinding not used.</td>
<td>143 patients (7 to 74) manifested with productive cough (mean duration 17 d)</td>
<td>1. Intervention: “Dai Zhe Zhi Sao San Jia Wei” (components: ruddle 30 g, inula flower 9 g, herba schizonepetae 9 g, swallowwort rhizome 9 g, aster root roasted 9 g, stemona root roasted 9 g, scutellaria root 9 g, platycodon root 6 g, tangerine peel 6 g, fresh licorice root 6 g, decocted twice for 800 mL extract), 400 mL, bid 2. Control: cephradine capsule 0.25 g qd, phenergan syrup (per 1000-mL mixture contains phenergan 1 g, glycerylguaiacolate 25 g, ammonium chloride 10 g, glucose 500 g) 10 mL tid</td>
<td>Marked improvement: all manifestations resolved within 7 days General improvement: all manifestations resolved, but relapsed once in a while during 14-day treatment Ineffective: no improvement with treatment of 14 days</td>
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<td>Wang 2001</td>
<td>Parallel design. Randomisation procedure unclear. Blinding not used. Allocation concealment unclear.</td>
<td>106 children (5 months to 12 years old) with fever and cough diagnosed with acute bronchitis</td>
<td>1. Intervention: Shi Wei Long Dan Hua Ke Li (components: gentian flower, savory rhododendron leaf, liquorice root, herba corydalis, unibract fritillary bulb, crab shell, costustoot), &lt;1 year 0.5 packet tid; 1 to 3 years 1 packet tid; 5 to 12 years 1.5 packet tid. 2. Control: amoxicillin, 10 mg/kg, tid or 15 mg/kg, bid</td>
<td>Marked improvement: fever, cough absent and feeling improved after 24-h treatment General improvement: symptoms improved after treatment within 48 hours Ineffective: not improved after treatment for 48 h</td>
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<td>Wang 2001</td>
<td>Parallel design. Randomisation procedure unclear. Blinding not used. Allocation concealment unclear.</td>
<td>556 patients manifested with cough, expectoration, pharynx itching diagnosed with acute bronchitis</td>
<td>1. Intervention: Zhi Sao San (component: epicarp citri, tatarian aster root, common coltsfoot flower, platycodon root, fineleaf schizonepeta herb and add other herbs according to manifest) 2. Control: Western medicine for antibiotics, antiviruses, preventing asthma and cough, and removing phlegm</td>
<td>Recovery: all symptoms and signs absent and no relapse within 2 weeks General improvement: cough and signs reducing Ineffective: no improvement after treated for two weeks.</td>
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Xu 2001


320 children diagnosed with acute bronchitis

1. **Intervention:** “Zi Ni San Ye Shuang Hua Tang” (components: hemsley rockvine root 6 g, mulberry leaf 6 g, perilla leaf 6 g, honeysuckle flower 6 g, chrysanthemum 6 g, placyodon root 6 g, fresh liquorice root 3 g, decocted for 100-mL extract which should be taken frequently each day)

2. **Control:** routine Western medicine for anti-inflammation

Marked improvement: symptoms absent or markedly improved
General improvement: symptoms improved
Ineffective: not improved

Yuan 2001


224 children (3 months to 14 years old) with cough and mean duration 3.1 days (9 hours to 6 days)

1. **Intervention:** “Xiao Er Xiao Ji Zhi Ke Kou Fu Ye” <1 year old 5 mL tid, 1 to 2 years old 10 mL tid, 3 to 4 years 15 mL tid, >5 years 20 mL tid

2. **Control:** cefotaxime sodium 50 to 100 mg/kg qd; fluimucil 1 year old 40 mg tid, 1 to 3 years 80 mg tid, 4 to 8 years 100 mg tid, >8 years 150 mg tid

Time of fever, cough, rhonchi, abdominal distention, halitosis, constipation, anorexia; Recovery: cough, fever, and signs of chest absence
General improvement: cough relief, respirations clear
Ineffective: no improvement or worse

Yuan 2002


82 children (1.5 to 13 years old) diagnosed with acute bronchitis

1. **Intervention:** ribavirin 10 to 15 mg/kg qd; penicillin 100 to 200 μg/kg qd; “E Shu You” glucose injection (components: oil of aromatic tumeric) 10 mL/kg qd; and remedy to symptoms

2. **Control:** ribavirin 10 to 15 mg/kg, qd; penicillin 100 to 200 μg/kg qd; and remedy to symptoms

Marked improvement: fever and cough resolved after 3-day treatment
General improvement: fever and cough improved but not absent
No effect: no improvement after 7-day treatment

Zeng 2002


231 patients (1 to 5 years old) manifested with cough, fever, anorexia, vomiting, diarrhea, hematose, rough respirations or inconstant rale or rhonchi, normal or abnormal radiographs, normal or abnormal white blood cell count. Excluded if temperature over 38°C, congenital heart disease, or tuberculosis

1. **Intervention:** amoxicillin of “Yu Xing Cao” Injection 2 mL bid; atomization, 40 mg/kg qid; phenergan syrup 5 mL tid

2. **Control:** Atomization of gentamicin 20 kilo units bid; Atomization, 40 mg/kg qid; phenergan syrup 5 mL tid

Time of each manifest resolved
Recovery: all manifest absence within 1 week
General effect: most manifest relief within 1 week 3-day treatment
No effect: no improvement

Zhai 2000


92 patients (16 to 64 years old) diagnosed with acute bronchitis

1. **Intervention:** “Zeng Xiao Zhi Ke He Ji” (components: roasted ephedra herb 10 g, apricot kernel 10 g, gypsum 30 g, liquorice root 10 g, honeysuckle flower 25 g, weeping forsythia 25 g, mulberry bark 10 g, blackberry lily rhizome 10 g, earthworm 10 g, indigowoad leaf 20 g, pepperweed seed 6 g, decocted for 100 mL extract), 50 mL bid, 100 mL bid, or 100 mL tid

2. **Control:** cefalexin 0.5 g qid

Recovery: all symptoms and signs absent
General improvement: symptoms and signs relieve
Ineffective: no improvement in symptoms and signs

(continued)
Zhang Parallel design. 120 patients diagnosed with acute bronchitis according to Practical Internal Medicine (Version 9).

1. Intervention: penicillin sodium 3,200,000 units bid; “Shuang Huang Lian” injection (components: honeysuckle flower, baical skullcap root, weeping forsythiae capsule) 3 to 3.6 g, qd to remedy symptoms
2. Control: penicillin sodium 3,200,000 units bid to remedy symptoms
Recovery: all manifests absence within 1 week
General improvement: most manifest relief within 1 week
No effect: no improvement
Adverse effect

Zhang Parallel design. 240 outpatients diagnosed with acute bronchitis according to Practical Pediatrics

1. Intervention: antibiotics and “Shi Wei Long Dan Hua Ke Li” (components: gentian flower, savory rhododendron leaf, liquorice root, herba corydalis, rhizoma codonopsis convolvulacea, unibract fritillary bulb, crab shell, costustoot) to remedy symptoms
2. Control: antibiotics
Time of fever, cough, phlegm, rhonchi

Zhang Parallel design. 250 children (1 to 12 years old) diagnosed with acute bronchitis

1. Intervention: cefotaxime sodium, “Jia Wei Zhi Sou San” (balloonflower root 10 g, fineleaf schizonepeta herb 10 g, tatarian Aster Root 10 g, tuber stemona root 10 g, glaucouscetum swallowwort rhizome 10 g, liquorice root 6 g, tangerine peel 6 g, honeysuckle flower 12 g, weeping forsythiae capsule 10 g, Great Burdock Achene 10 g, blackberry lily rhizome 10 g, apricot kernel 6 g, commoncoltsfoot flower 10 g, divaricate saposhnikovia root 6 g, decocted for extract, p.o. bid)
2. Control: cefotaxime sodium
Recovery: all symptoms and signs absent
Marked improvement: marked relief of symptoms and signs
General improvement: relief of symptoms and signs
No effect: no improvement in symptoms and signs

Zhou Parallel design. 230 patients 6 months to 12 years presented with cough, rough respirations, or rhonchi

1. Intervention: “Yu Xing Cao” injection (extract of heart leaf houttuynia herb) 6 months to 3 years: 10 mL qd; <8 years: 20 mL qd; <12 years: 30 mL qd penicillin/cefalexin to remedy symptoms
2. Control: penicillin/cefalexin to remedy symptoms
Marked improvement: cough, rough respirations, or rhonchi resolved after 1-day treatment
General improvement: cough relieved and rough respirations or rhonchi resolved after 3-day treatment
Ineffective: no improvement after 5-d treatment

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<td>1. Intervention: penicillin sodium 3,200,000 units bid; “Shuang Huang Lian” injection (components: honeysuckle flower, baical skullcap root, weeping forsythiae capsule) 3 to 3.6 g, qd to remedy symptoms</td>
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<td>Zhang 2003</td>
<td>Parallel design. Randomisation procedure unclear. Blinding not used. Allocation concealment unclear.</td>
<td>250 children (1 to 12 years old) diagnosed with acute bronchitis</td>
<td>1. Intervention: cefotaxime sodium, “Jia Wei Zhi Sou San” (balloonflower root 10 g, fineleaf schizonepeta herb 10 g, tatarian Aster Root 10 g, tuber stemona root 10 g, glaucouscetum swallowwort rhizome 10 g, liquorice root 6 g, tangerine peel 6 g, honeysuckle flower 12 g, weeping forsythiae capsule 10 g, Great Burdock Achene 10 g, blackberry lily rhizome 10 g, apricot kernel 6 g, commoncoltsfoot flower 10 g, divaricate saposhnikovia root 6 g, decocted for extract, p.o. bid)</td>
<td>Recovery: all symptoms and signs absent. Marked improvement: marked relief of symptoms and signs. General improvement: relief of symptoms and signs. No effect: no improvement in symptoms and signs.</td>
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<td>Zhou 2003</td>
<td>Parallel design. Randomisation procedure unclear. Blinding not used. Allocation concealment unclear.</td>
<td>230 patients 6 months to 12 years presented with cough, rough respirations, or rhonchi</td>
<td>1. Intervention: “Yu Xing Cao” injection (extract of heart leaf houttuynia herb) 6 months to 3 years: 10 mL qd; &lt;8 years: 20 mL qd; &lt;12 years: 30 mL qd penicillin/cefalexin to remedy symptoms</td>
<td>Marked improvement: cough, rough respirations, or rhonchi resolved after 1-day treatment. General improvement: cough relieved and rough respirations or rhonchi resolved after 3-day treatment. Ineffective: no improvement after 5-d treatment.</td>
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FIG. 1. Time to improvement of symptoms and signs. Except one study,28 Chinese herbal medicines of other 11 studies appeared statistically significantly fewer time to improvement of symptoms and signs than control remedies.

1. Xiao’er Xiao Ji Zhi Ke Kou Fu Ye versus cefotaxime plus fluimucil (N-acetylcysteine)25 Time to resolution of cough was evaluated and showed a statistically significant decrease (WMD −0.62 days, 95% CI −1.12 to −0.12).

2. Yu Xing Cao atomization versus gentamicin atomization.27 Time to relief of cough was evaluated and showed a statistically significant decrease (WMD −1.37 days, 95% CI −1.67 to −1.07).

FIG. 2. Improvement in signs and symptoms. Seven studies appeared that significantly more participants were improved in symptoms and signs in Chinese herbal medicines treatment group than in control group.
3. Wheezing: Data from one trial showed that the duration of wheezing was shorter in the Chinese herbs group than in the control group.

1. Xiao'er Xiao Ji Zhi Ke Kou Fu Ye versus cefotaxime plus fluimucil (N-acetylcysteine)\(^2\)
   Time to resolution of wheezing was evaluated and the decrease in time showed statistical significance (WMD = -0.99 days, 95% CI = -1.44 to -0.54).

2. Yu Xing Cao atomization versus gentamicin atomization\(^2\)
   Time to resolution of wheezing was evaluated and the decrease in time showed statistical significance (WMD = -3.17 hours, 95% CI = -34.81 to -29.45).

Improvement in symptoms and signs (Fig. 2)

1. Cough: Data from two trials showed that patients with cough received greater relief in the Chinese herbs group than in the control group.
   (1) Xiao'er Xiao Ji Zhi Ke Kou Fu Ye versus cefotaxime plus fluimucil (N-acetylcysteine)\(^2\)
   The proportion of patients with cough resolved at follow-up showed statistical significance (RR 1.28, 95% CI 1.01 to 1.61).
   (2) Shi Wei Long Dan Hua Ke Li plus antibiotics versus antibiotics\(^2\)
   The proportion of patients with cough relieved by treatment showed statistical significance (RR 1.42, 95% CI 1.05 to 1.49).

2. Fever: Data from two trials showed that patients with fever received greater relief in the Chinese herbs group than in the control group.
   (1) Xiao'er Xiao Ji Zhi Ke Kou Fu Ye versus cefotaxime plus fluimucil (N-acetylcysteine)\(^2\)
   The proportion of patients with fever resolved at follow-up showed statistical significance in favor of Chinese herbs (RR 5.15, 95% CI 3.16 to 8.41).
   (2) Shi Wei Long Dan Hua Ke Li plus antibiotics versus antibiotics\(^2\)
   The proportion of patients with fever relieved by treatment showed statistical significance in favor of Chinese herbs (RR 1.27, 95% CI 1.07 to 1.49).

3. Chest film: One trial comparing Tan Re Qing injection to levofloxacin\(^1\) showed a greater number of patients with normal chest film in the Chinese herbs group than in the control group (RR 1.28, 95% CI 1.01 to 1.61).

4. Rales: Data from one trial showed that patients with rales received greater relief in the Chinese herbs group than in the control group. This difference showed statistical significance for both moist rales (RR 1.23, 95% CI 1.05 to 1.46) and dry rales (RR 1.23, 95% CI 1.03 to 1.46).

Ineffective treatment, by global assessment at follow-up (Fig. 3)

Data for ineffectiveness rates were available from 13 trials. The reduction in ineffectiveness with Chinese herbs showed statistical significance in nine trials (RR 0.24, 95% CI 0.07 to 0.80\(^2\); RR 0.16, 95% CI 0.08 to 0.34\(^3\); RR 0.07, 95% CI 0.01 to 0.49\(^2\); RR 0.25, 95% CI 0.10 to 0.65\(^2\); RR 0.23, 95% CI 0.10 to 0.54\(^4\); RR 0.22, 95% CI 0.07 to 0.71\(^5\); RR 0.17, 95% CI 0.04 to 0.72\(^6\); RR 0.20, 95% CI 0.06 to 0.67\(^7\); RR 0.40, 95% CI 0.17 to 0.97\(^8\)).

No statistical significance was evident in four trials (RR 0.55, 95% CI 0.21 to 1.39\(^9\); RR 0.45, 95% CI 0.20 to 1.01\(^10\);
RR 0.64, 95% CI 0.31 to 1.34; RR 0.42, 95% CI 0.17 to 1.06.

**Adverse events**

One trial reported on adverse effects during treatment. One (1) patient treated with *Huang Huang Lian* injection complained about a skin rash, which disappeared when treatment was stopped.

**DISCUSSION**

Since there is no gold standard test, the diagnosis of acute bronchitis must be based on clinical assessment. All of the trials in the review included patients with recent onset of a respiratory illness with productive cough and fever and excluded patients with chronic pulmonary disease. The clinical characteristics of the enrolled patients varied but were consistent with the variety of similar definitions generally used by primary physicians. Therefore, these results appear to be generalisable to the management of acute bronchitis in community practices.

Four trials reported the time to improvement of cough, fever, and rales and showed that patients treated with Chinese herbs had a shorter duration of signs and symptoms. Two trials reported the proportion of patients with improved signs and symptoms at follow-up and showed that Chinese herbs were beneficial for the relief of signs and symptoms.

The majority of trials reported data on physician global assessment of improvement at follow-up. Regarding ineffective rates, nine out of 13 trials showed that Chinese herbs were superior to routine treatment; and the other four trials showed a similar effect to routine treatment. In general, Chinese herbs appeared more beneficial.

In this review 12 preparations of Chinese herbs were assessed. The numbers of included trials using the same preparation were very few. In addition to the low quality of the included trials, the conclusions were inadequate. Furthermore, many trials did not give adequate information about the control group, just referring to “antibiotics,” “antiviral,” “antitussive,” et cetera. The specific drug name and the dosages were not mentioned. For example, in three trials *Shi Wei Long Dan Hua Ke Li* was administered.

**FIG. 3.** Ineffective treatment, by global assessment at follow-up. Except in four studies, nine studies showed that significantly fewer people lacked effect than those who were treated by Chinese herbal medicines rather than control remedies.
to the intervention group and antibiotics were administered to both the intervention and control groups, but which antibiotic was used was not described.

In one (1) of 14 trials adverse events were reported, in the Shuang Huang Lian injection plus penicillin-group only. Some studies described any adverse events with Chinese herbs in terms of “safety” or “low side-effect,” but these statements were not supported with adequate data.

The majority of studies did not give adequate methodological information. None of the studies mentioned allocation concealment, which could prevent selection bias. All trials mentioned random allocation but did not state the method used. We contacted the authors to elicit the methods used and discovered some errors.

The majority of studies were of low quality and without double-blinding, which may result in bias. Blinding was not mentioned in all of the trials. Chinese herbal preparations are usually different in terms of appearance, taste, and smell to Western medicines. Therefore, blinding was difficult. Some injection preparations, for example, Tan Re Qing injection, could be blinded to patients and operator but blinding was not used. None of the studies mentioned blinding of the outcome assessors, leading to suspicion of detection bias. Publication bias may exist as all the included studies were published in Chinese and no primary article reported negative results.

The outcome definition and timing of outcome measures varied from study to study; in addition, there were only a small number of trials for each preparation. It was difficult to do a meta-analysis, which has led to some loss of information. The outcome definitions adopted by this review and used in the majority of studies were based on the period and extent of cough, fever, and other manifestations, which may lead to diversities of subjective judgement by individual physicians. There was also a loss of information from the studies that did not provide the data to fulfill the outcome criteria stipulated by this review. A more objective definition of outcome measures may be adopted in future updates of this review. The disease duration at trial entry also varied between studies.

This review may be affected by selection bias, performance bias and detection bias due to lack of allocation concealment and blinding. Meanwhile, bias may have occurred due to the limited number of small trials.

CONCLUSIONS

Implications for practice

There are insufficient quality data to recommend the routine use of Chinese herbs for acute bronchitis. The benefit found in individual studies and this systematic review could be due to publication bias and study-design limitations. In addition, the safety of Chinese herbs is unknown due to the lack of toxicological evidence on these Chinese herbs, though adverse events were rarely reported. Chinese herbs should be used carefully.

Implications for research

There is a widespread belief among Chinese clinicians and patients that Chinese herbs are effective in improving signs and symptoms of acute bronchitis. Due to the low quality of trials, this conclusion is unreliable. This demands that additional, well-designed randomised controlled trials with adequate power to provide a definitive answer need be conducted. For many Chinese researchers, allocation concealment should be emphasised and the approaches should be reported clearly. Randomisation procedure also should be described clearly in reports. Blinding should be conducted in trials on Chinese herbs, though this may be difficult. Studies should emphasise adverse effects, and more toxicological research on Chinese herbs should be conducted, which would provide important information for clinicians.

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Address reprint requests to: Taixiang Wu, M.Sc.
Chinese Cochrane Centre
International Clinical Epidemiology Network (INCLEN)
Research and Training Center
West China Hospital
Sichuan University
No. 37, Guo Xue Xiang
Chengdu 610041
China
E-mail: txwutx@hotmail.com