Efficacy of Chinese herbal medicine for lumbar disc herniation: a systematic review of randomized controlled trials

Yi Luo, Jian Huang, Lin Xu, Weikang Zhao, Jie Hao, Zhenming Hu

Abstract

OBJECTIVE: This is a review of the effects of Chinese herbal medicine (CHM) used alone to treat lumbar disc herniation (LDH).

METHODS: A literature search of the following electronic databases from their inception to February 2013 was conducted: Chinese Biomedical databases, Chinese National Knowledge Infrastructure, Wanfang Database, China Science and Technology Journal Database, Cochrane Library, Web of Science, MEDLINE, and EMBASE. Randomized controlled trials where CHM had been used to treat LDH were selected. Data extraction, quality assessment, and data analysis were carried out by two independent reviewers.

RESULTS: Of the 2415 studies identified, eight with complete data on 1146 patients were selected. The methodological quality was poor in all trials. Five studies reported that CHM was better than Western Medicine [OR=2.81, 95% CI (1.27, 6.18); OR=3.34, 95% CI (1.92, 5.79); OR=2.22, 95% CI (1.08, 4.57); OR=6.67, 95% CI (1.34, 33.28); and OR=1.94, 95% CI (1.23, 3.06)]. Two studies reported that the clinical outcome was better in CHM groups than in physiotherapy and placebo groups, [OR=3.02, 95% CI (1.08, 8.46); and OR=2.67, 95% CI (1.26, 5.64), respectively], whereas one study reported no difference between CHM and physiotherapy groups. One study reported that CHM resulted in higher Japanese Orthopedic Association scores [MD=7.78, 95% CI (6.67, 8.89)] than in a control group and another that participants treated with CHM had lower Visual Analogue Scale scores [MD= - 0.72, 95% CI ( - 0.91, - 0.58)] than those in a control group. Three studies reported that the adverse effects of CHM and Western Medicine did not differ significantly [OR=0.10, 95% CI (0.01, 1.85); OR=0.19, 95% CI (0.01, 4.07); and OR=0.07, 95% CI (0.00, 1.32)].

CONCLUSION: CHM may be more effective than other interventions for LDH; however, methodological weaknesses in the studies assessed in this review prevent a definitive conclusion. More high-quality large-scale studies are required to clarify this matter.

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Key words: Drugs, Chinese herbal; Review; Randomized controlled trial; Lumbar disc disease

INTRODUCTION

Displacement of the lumbar disc beyond a damaged annulus fibrosus is defined as lumbar disc herniation
LDH). Its prevalence is about 1%-3% in European countries. The highest incidence is among people aged 30-50 years and the ratio of male to female is 2:1. The commonest symptoms caused by LDH are lower back pain (LBP) and sciatica (a specific subgroup of LBP). It imposes an economic burden on patients because of their frequent absences from work.

Some conventional treatments for LBP, including various surgical treatments, non-steroidal anti-inflammatory drugs (NSAIDs), neurotrophics, and dehydrating drugs, have positive effects. However, some adverse effects of Western Medical treatments are unavoidable. The risk of gastrointestinal bleeding with NSAIDs is high in elderly patients. In the practice of Traditional Chinese Medicine (TCM), Chinese herbal medicine (CHM) has long been used to treat LDH. In terms of TCM theory, LDH is known as “Yao Bi” and is usually caused by blood stasis and Qi stagnation, cold-dampness, or deficiencies in liver and kidney function.

Recently, the effectiveness of CHM for treating LDH has been reported widely. However, many of these studies did not evaluate the effects of CHM used alone. The present systematic review aimed to use evidence from published randomized clinical trials to evaluate the efficacy of CHM used alone to treat LDH.

METHODS

Search strategy

Domestic databases, including the Chinese Biomedical databases, Chinese National Knowledge Infrastructure, Wanfang database, and China Science and Technology Journal database (CSTJ), were searched. The overseas databases searched included the Cochrane Library, Web of Science, MEDLINE, and EMBASE. All databases were searched from inception up to February 2013. Papers presented at the International Congress of the Chinese Orthopedic Association from its inception up to 2012 were also manually searched. Unpublished studies were identified using Google. The terms used for searching were as follows: (a) low back pain; (b) lumbar disc degeneration; (c) spinal diseases; (d) lumbar disc herniation; (e) 1 or 2 or 3 or 4; (f) alternative medicine; (g) herb; (h) Chinese herbal medicine; (i) nonprescription drug; (j) botanical; (k) 6 or 7 or 8 or 9 or 10; (l) controlled clinical trial; (m) randomized controlled trial; (n) randomized; (o) placebo; (p) randomly; (q) trial; (r) 12 or 13 or 14 or 15 or 16 or 17; (s) 5 and 11 and 18.

Inclusion criteria

Types of study: all randomized controlled trials related to LDH were included, regardless of language.

Types of participant: adult patients with a definite diagnosis of LDH. Patients with other diseases, such as trauma, tumor, fracture, infection, muscle strain, or spinal deformity, were excluded.

Types of intervention: the treatment groups included only used CHM/formulae either internally or externally or both. The control groups used other treatments such as placebos and Western Medicine-type medications. Studies in which CHM was used in the control groups were excluded, as were those that used non-Chinese herbal medicines.

Types of outcome measure: outcome measures were clinical efficacy, adverse effects, Japanese Orthopedic Association (JOA) scores, and Visual Analogue Scale (VAS) scores.

Data extraction and assessment

All articles were identified by the specific search strategies described above. Two reviewers (Luo and Huang) assessed the articles independently. Any disagreements were resolved by a third reviewer (Hu). Similarly, the data were independently extracted by two researchers (Luo and Huang) according to the defined criteria and differences of opinion resolved by the third reviewer (Hu). Figure 1 is a flow chart depicting the selection process and the reasons for exclusion.

The risk of bias was evaluated using the Cochrane Collaboration’s risk of bias criteria, which are as follows: (a) random sequence generation; (b) allocation concealment; (c) blinding of participants and personnel; (d) blinding of outcome assessment; (e) incomplete outcome data; (f) selective reporting; and (g) other biases. Two of the authors (Luo and Huang) independently evaluated the quality of the studies and consulted with the other authors when their viewpoints differed.

Data analysis

The program Revman 5.1 (Cochrane Collaboration, Oxford, UK) was used to compare the outcomes of the treatment groups with the control groups for all statistical analyses. Odds ratio (OR) were used to compare dichotomous data and mean differences (MD) to compare continuous variables and 95% confidence intervals (CI) calculated for them. Meta-analyses were performed where the interventions were comparable and the heterogeneity low. Heterogeneity was assessed based on the $\chi^2$ test. A random effects model was used for meta-analysis where there was significant heterogeneity ($P<0.10$) and a fixed effects model where there was not significant heterogeneity ($P\geq0.10$).

RESULTS

Study selection and characteristics

In total, 2415 studies were retrieved using the search terms. Of these studies, 1351 were in English and 1064 in Chinese. One hundred and four studies were excluded because of duplication and a further 2238 after reading their titles and abstracts. An additional 453 studies were excluded because they were not relevant to LDH, 726 studies because they were not relevant to
CHM, 188 studies because they were not clinical trials, 845 studies because multiple inventions had been performed in both control and treatment groups, and 26 studies because they were reviews. The full texts of the remaining 73 studies were obtained for further evaluation, after which 65 of them were excluded based on our evaluation of the detailed data: 36 because CHMs were used in the control group, 17 because there were multiple inventions in the treatment groups (not noted in the abstracts), and 12 because they were not randomized controlled trials (Figure 1). Finally, eight studies remained, all of which had been published in Chinese journals and performed in China. These eight trials involved 1146 patients in total (Table 1).

### Study quality

Only two of the studies used an appropriate sequence generation method. None of the studies reported

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**Table 1** Characteristics of assessed studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Case</th>
<th>Inclusion criteria</th>
<th>Age (years)</th>
<th>Treatment</th>
<th>Control</th>
<th>Course (days)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ye KX 2006</td>
<td>60</td>
<td>CT and MRI</td>
<td>18-70</td>
<td>Jingyao tong decoction</td>
<td>Lumbar traction</td>
<td>28</td>
<td>CR</td>
</tr>
<tr>
<td>Diao JH 2008</td>
<td>108</td>
<td>CT and MRI</td>
<td>23-56</td>
<td>Yaotong huxue capsule</td>
<td>Meloxicam</td>
<td>14</td>
<td>CR</td>
</tr>
<tr>
<td>Li CJ 2009</td>
<td>240</td>
<td>Practical Orthopaedics</td>
<td>24-55 Control: 34.4 Treatment: 33.3</td>
<td>Jingyao tong capsule</td>
<td>Ibuprofen</td>
<td>30</td>
<td>CR</td>
</tr>
<tr>
<td>Chen FH 2011</td>
<td>120</td>
<td>Criteria of Diagnostic and Therapeutic Effect of Chinese Medicine for Disease Manipulations of Diagnostic and Therapeutic Effect of Chinese Medicine</td>
<td>20-70</td>
<td>Biechong chubi capsule</td>
<td>Placebo</td>
<td>15</td>
<td>CR, JOA</td>
</tr>
<tr>
<td>Ma YX 2011</td>
<td>68</td>
<td>CT and MRI</td>
<td>30-60</td>
<td>Duhuo jishen decoction</td>
<td>Diclofenac sodium</td>
<td>21</td>
<td>CR, AE</td>
</tr>
<tr>
<td>Zhao CW 2010</td>
<td>116</td>
<td>CT and MRI</td>
<td>21-65</td>
<td>CHM hot compress</td>
<td>Electromagnet wave</td>
<td>20</td>
<td>CR</td>
</tr>
<tr>
<td>Wang LX 2012</td>
<td>310</td>
<td>CT and MRI</td>
<td>26-70</td>
<td>Duhuo jishen decoction</td>
<td>Diclofenac sodium</td>
<td>21</td>
<td>CR, AE</td>
</tr>
</tbody>
</table>

Notes: CHM: Chinese herbal medicine; CR: curative rate; AE: adverse effects; JOA: Japanese orthopedic association scores; VAS: visual analogue scale.

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Figure 1 Flow diagram showing selection procedure

LDH: lumbar disc herniation; CHM: Chinese herbal medicine; RCTs: randomized controlled trials.
ed allocation concealment or blinding and none reported complete outcomes (Figures 2 and 3).

Assessment of outcomes
The rate of cure was used as an indicator of clinical efficacy in all of the assessed studies.7-14 One study8 used the Manipulations of Diagnostic and Therapeutic Effect of Chinese Medicine, six used the Criteria of Diagnostic and Therapeutic Effect of Chinese Medicine for Disease, and the remaining one14 used criteria devised by the author. Based on these criteria, outcomes were allocated to one of four levels: cure, significantly effective, effective, and ineffective. Rate of cure was to be calculated from the number of cured cases (first level); however, this meta-analysis was abandoned because the assessed studies were too clinically diverse, with variable types of intervention and different treatment courses.

Curative rate
Five studies5,9,10,12,14 compared CHM with Western Medicine, two compared CHM with physiotherapy, and one compared CHM with placebo. In seven studies,2-7,10,12,14 the CHM groups had a higher rate of cure than the control groups. One study reported no difference between CHM and physiotherapy (Figure 4).

JOA scores
In the one study11 that used JOA scores, these scores were higher in the CHM group than in the control group [MD=7.78, 95% CI (6.67, 8.89)].

VAS scores
In the one study14 that used VAS scores, these scores were lower in the CHM group than in the control group [MD= -0.72, 95% CI (-0.86, -0.58)].

Adverse effects
Three studies7-12,14 reported adverse effects, specifically stomach discomfort. All three studies reported no differences between the CHM and control groups in adverse effects (Figure 5).

Publication bias
Funnel plots produced to assess publication bias showed an asymmetrical distribution (Figure 6). Thus, there is a publication bias in our review.

DISCUSSION
Our review shows that CHM therapy alone produces a better clinical outcome than other therapies in patients with LDH. There was no difference between CHM and Western Medicine in terms of the risk of adverse effects. However, methodological limitations compromise the reliability of these conclusions.
Reasons for the possible effectiveness of CHM

Experimental studies have shown that CHMs may help to prevent degeneration of the lumbar disc and that they have analgesic effects. The mechanisms that underlie the effects of CHM in LDH remain unknown; however, CHM are known to have significant anti-inflammatory effects. In animal models, Yaotuítong capsules reportedly significantly reduce prostaglandin E2 and 5-hydroxytryptamine concentrations in injured nerve roots. CHM can increase type II collagen concentrations and decrease expression of metalloproteinase 3, metalloproteinase 13, and interleukin-1β in degenerated discs. These studies may explain why CHM both relieves the symptoms of LDH and also prevents disc degeneration.

According to TCM theory, development of LDH is attributable to deficiencies of the kidney, injuries, and invasion by exogenous pathogenic wind, cold, and dampness. Because invasion of exogenous adverse elements and injury block the meridian, patients experience pain. Drugs that improve blood circulation, such as Ruxiang (Olibanum), Moyao (Myrrh), Danggui (Radix Angelicae Sinensis), and Chuanxiong (Rhizoma Chuanxiong), have beneficial effects. In addition, Qi-tonifying drugs, such as Duzhong (Cortex Eucommiae), Niuxi (Radix Achyranthis Bidentatae), Huangqi (Radix Astragalii Mongolici) and Wujiaipi (Cortex Acanthopanacis Radici), which improve kidney function or strengthen bones, are also effective.

Limitations of the evidence

This review has some drawbacks because of the following limitations in the studies assessed. (a) All the studies were written in Chinese and published in Chinese journals. Positive results of clinical research related to CHM are more likely to be published in China. Thus, a publication bias was inevitable and this was indeed present according to our funnel plots. (b) Only two studies described an appropriate random sequence generation procedure using a random number table. Thus, these studies had a high risk of selection bias. (c) Performance bias and detection bias were not considered in these studies. Blinding is very important for protecting against bias and ensuring that valid results are obtained. Regrettably, all eight assessed studies were un-
clear about blinding of participants and personnel and blinding of outcome assessments. Thus, the likelihoods of performance biases and detection biases were high. (d) None of the studies mentioned attrition or withdrawal rates. Intention-to-treat analyses were not performed in any of the studies assessed. Thus, it is possible that there was a high risk of attrition bias. Overall, our findings therefore provide limited evidence on this topic.

How does this review differ from other reviews?
Several systematic reviews of CHM have reported similar findings on this topic. A systematic review of a Duhuoqisheng decoction included various studies; however, in these studies, the treatment groups received CHM combined with other therapies. With the aim of evaluating the efficacy of CHM alone in the treatment of LDH, we only included studies in which the treatment group received CHM alone. Although their methodological quality was low, the studies we identified did provide some information that is relevant to clinical practice. Studies of LBP treatment with herbal medicines performed outside China have been included in previous systematic reviews. However, the herbal medicines used in those studies are not the same as those used in CHM and those studies were only included to guide basic research and clinical treatments. We excluded clinical studies of herbal medicines that were not guided by TCM theory.

Recommendations for future clinical research and practice
Future studies should describe their randomization procedures in greater detail, perform allocation concealment as far as possible, apply a blinding method during the assessment procedure, and report intention-to-treat analyses. There is a need for large clinical trials to test the efficacy of CHM. We recommend that CHM should be combined with other LDH therapies, such as Western Medicine and physiotherapy.

CONCLUSION
According to our review, CHM had beneficial effects on LDH. However, we did identify some methodological defects that weakened the reliability of our conclusions. In spite of this limitation, our findings might inform future clinical practice and research.

REFERENCES