Evaluation of different moxibustion doses for lumbar disc herniation: multicentre randomised controlled trial of heat-sensitive moxibustion therapy

Mingren Chen,1 Rixin Chen,1 Jun Xiong,1 Zhenhai Chi,1 Jianhua Sun,2 Tongsheng Su,3 Meiqi Zhou,4 Fan Yi,1 Bo Zhang1

Abstract

Background There is some evidence for the effectiveness of moxibustion for the treatment of lumbar disc herniation (LDH), but it remains unclear what dose is optimal.

Objective To compare the effectiveness of a new technique of individualised ‘sensitivity elimination’ dose versus a standardised 15 min dose in the treatment of LDH.

Methods This study was a multicentre (four centres in China), randomised, controlled trial with two parallel arms (group A, individualised sensitivity elimination dose; group B, standardised dose). The most heat-sensitive acupuncture point from the triangle bound by BL25 and GV2 was selected. Both groups received 18 sessions over 2 weeks. The outcome was evaluated by Modified Japanese Orthopaedic Association scale (M–JOA) score before and after treatment and at 6-month follow-up examination. All main analyses were by intention to treat.

Results A total of 96 patients were included. A significant difference of total M–JOA score was noted between the groups at weeks 1 and 2 (p<0.05). Significant differences were also evident during the follow-up period (p<0.01). The mean duration of moxibustion was 42.7±5.4 (range, 22–58) minutes in the experimental group.

Conclusions The effectiveness of the individualised sensitivity elimination dose appears superior to the standardised dose in the treatment of LDH. Only 15 min moxibustion in the conventional dose group seemed insufficient to elicit the satisfactory clinical effects obtained by heat-sensitive moxibustion therapy. However, in view of some limitations of this study further research is necessary before this can be stated conclusively.

Trial Registration Controlled Clinical Trials: ChiCTR-TRC-09000602.____

BACKGROUND

Heat-sensitive moxibustion therapy is a common method of ‘suspended moxibustion’ treatment in China.1 Suspended moxibustion is a traditional Chinese medical intervention that involves burning of moxa indirectly at the acupuncture points. Moxibustion has anti-inflammatory and immunomodulatory effects against chronic inflammatory conditions in humans.2 Moxibustion as treatment of lumbar disc herniation (LDH) exerts diverse therapeutic effects and its mechanisms are suggested by the observations that moxibustion can improve local blood circulation, eliminate nerve root inflammation and oedema, soften adhesions and reduce protrusion of the nerve root, thereby promoting nerve injury repair.3 Moreover, the heat of moxa treatment improves microcirculation in the lumbar vertebrae.4

The treatment may be used for various diseases in one particular way, at ‘heat-sensitised’ acupuncture points. In humans, it is believed that there are two states of acupuncture points, that is, the sensitised or ‘awake’ state and the resting state. According to this theory, in the presence of disease, acupuncture points on the body surface are stimulated and become sensitive. The sensitive areas are susceptible to heat stimulation and called ‘heat-sensitised points’. One of the characteristics of these areas is that they are specific or closely related to acupuncture points, and behave similarly in clinical observations, that is, ‘small stimulation induces a large response’.

Thus, according to the current theory of heat-sensitive moxibustion, disease within the body can be reflected in acupuncture points of the body surface.1 We have identified this phenomenon in certain areas in patients with LDH. The triangular region bordered by bilateral Dachangshu (BL25) and Yaoshu (GV2) is the most common. Several articles have reported the effectiveness and safety of heat-sensitive moxibustion for LDH.5–9

Unlike acupuncture stimulation, which involves thrusting or twisting needles resulting in various biochemical reactions that can have effects throughout the body, moxibustion uses heat stimulation at various temperature levels from mild skin warming to tissue
damage from burning. The dose of moxa plays an important role in obtaining good effects. The regimen of moxibustion used for treatment of LDH has varied among studies, essentially in two main regimens. One uses a standardised dose, recommended by a widely accepted textbook: moxa is applied for 15 min per acupuncture point. The other regimen considers that the dose should differ according to patients’ condition and moxibustion sensation. Treatment sessions only end when patients feel that the acupuncture point heat-sensitisation phenomenon has disappeared. We called this the ‘individualised sensitivity elimination dose’.

It would be valuable to know whether the use of fixed dose is as effective as that of an individualised approach. We planned a rigorous multicentre, randomised controlled trial to seek for optimal dose model of the best therapeutic effect.

METHODS

Design
A multicentre, randomised, assessor blinded, controlled trial was conducted at four centres in China: the Affiliated Hospital with Jiangxi University of Traditional Chinese Medicine (TCM), Nanchang, First Affiliated Hospital with Anhui University of TCM, Hefei, Jiangsu TCM Hospital, Nanjing, and Shanxi TCM Hospital, Xian. The study was sequentially conducted as follows: a run-in period of 1 week prior to randomisation, a treatment period of 14 days and a follow-up period of 6 months. At the end of the run-in period, participants were randomised to the individualised sensitivity elimination dose group or the standardised dosage group by a central randomisation system (CRS) provided by China Academy of Chinese Medical Sciences, which adopted computer telephone integration technology to integrate computer, internet and telecom. The random number list was assigned by interactive voice response (IVR) and interactive web response. The CRS is a web-based electronic system used to screen and enrol patients. The CRS presented a site status page that listed all screened patients. Each entered patient was assigned a unique screening number. Patients that were randomised and assigned a computer generated code from the CRS.

Researchers who did not participate in the treatment and who were blinded to the allocation results performed the outcome assessment.

Sample size
We wanted to estimate the sample size that would suffice to detect differences of Modified Japanese Orthopaedic Association scale (M-JOA; see website) between the two groups. On the basis of a pilot study, the SD of the M-JOA score was set at 4.24 and a mean difference between groups of 2.47 was considered relevant. It was calculated that 80 patients were needed to obtain statistical power >90% and a significance level 0.05 in both outcomes. We estimated a dropout rate of 20%; therefore we aimed to recruit 96 patients.

Participants

Recruitment
A total of 96 eligible patients were enrolled in the study between September 2009 and March 2010. Recruitment strategies included dissemination of information on the study through newspapers, television, advertisements, signs posted at university-affiliated hospitals, and letters to local LDH support groups and healthcare providers with large caseloads of patients with LDH. Potential participants were informed that they had an equal chance of being assigned to one of two moxibustion interventions.

Inclusion criteria
 Eligible participants were those previously diagnosed as having moderate-to-severe LDH according to the M-JOA criteria (score, >10). Patients were required to complete the baseline LDH diary. Written informed consent was obtained from each participant. Diagnosis was made according to the following criteria: (1) pain occurring in lower back and radiating to lower limb; (2) straight leg raising test positive; (3) computed tomography (CT) suggestive of disc herniation; (4) skin sensation, such as tingling (a ‘pins-and-needles’ sensation) or numbness in a part of one leg; (5) muscle weakness or atrophy in later stages; (6) a loss of deep tendon reflexes in the lower extremities; (7) changes in spinal posture; (8) lateral lumbar spine x-ray films showing scoliosis or lumbar lordosis. The first three items were essential inclusion criteria, the other items were optional. The above criteria mainly derived from the guiding principles of clinical research on new drugs.

Because the research involved moderate-to-severe or severe LDH, the inclusion criteria also included the following: the triangle region formed by bilateral BL25 and GV2 (Dachangshu-Yaoshu-contralateral Dachangshu intraregion) had to reveal heat-sensitive points. Participants were instructed to stop LDH symptomatic relief medication during the run-in and treatment periods and provided usual care instruction for LDH.

Exclusion criteria

Participants were excluded if they had serious life-threatening disease such as disease of the heart and brain, blood vessels, liver, kidney and haematopoietic system, and psychosis. Women participants who were pregnant or lactating were ineligible. The following conditions were also excluded: single nerve palsy or cauda equina nerve palsy manifested as muscle paralysis or rectum or bladder symptoms; complication with lumbar spinal canal stenosis and space-occupying lesions for other reasons; complication with lumbar spine tumours, infections, tuberculosis, and so on; moxibustion syncope and unwilling to be treated with moxibustion; no written informed consent.

Study interventions
Moxibustion was performed by certified acupuncture medical doctors at four centres. Qualified specialists of
acupuncture in TCM with ≥5 years’ clinical experience performed moxibustion in this study. All treatment regimens were standardised among practitioners at the four centres by video, hands-on training and internet workshops.

In the two groups 22 mm (diameter) × 120 mm (length) moxa-sticks (Jiangxi TCM Hospital, China) were used. Patients were usually in the comfortable prone position for treatment, at a room temperature 24–30°C.

Individualised sensitivity elimination dose group

In the individualised sensitivity elimination dose group, moxa-sticks were lit by the therapist and held over the region comprising BL25 and GV2. The moxa-stick suspended at an approximate distance of 3 cm was used to search for acupuncture points showing the heat-sensitisation phenomenon. The areas were given mild warmth without burning by moxa-sticks, which was maintained until the patient reported the characteristic heat sensitisation sensation, said to indicate effective moxibustion, that is commonly called ‘de qi’. Patients felt comfortable throughout the moxibustion manipulation.

The following sensation indicated the presence of a heat sensitisation acupuncture point: ‘diathermic’ sensation due to moxa heat, defined as heat sensation conducting from the local skin surface into deep tissue, or even into the abdomen; ‘expanding’ sensation defined as the heat sensation spreading to surrounding area little by little around the moxa point; ‘transferred’ sensation defined as the heat sensation transferring along some pathway or direction. When such an acupuncture point was found, the therapists marked the point. We explored the whole area to find all heat-sensitive points.

After obtaining the heat sensitisation sensation, the therapists began to treat patients at the most heat-sensitive intensity acupuncture point. The moxibustion was continued as long as the patient reported heat sensitivity. One acupuncture point was stimulated during each session. The moxa stick also held steadily at the 3 cm distance using a device used to fix the moxa-sticks (figure 1).

Figure 1 Device holding moxa stick at fixed location.

Treatment sessions ended when patients felt the acupuncture point heat-sensitisation phenomenon had disappeared. Heat sensitivity tended to reduce over the course of treatment, but could always be identified even at the end of treatment. After each treatment, the therapist recorded the duration of moxibustion. Patients received treatment twice/day in week 1 then once/day starting from week 2 for a total of 18 sessions over 14 days.

Standardised dose group

Patients in the standardised dose group received treatment identical to the individualised group except that the duration was 15 min. Likewise, patients received the treatment twice/day in week 1 then once/day starting from week 2 for a total of 18 sessions over 14 days.

Outcome measures

The JOA has proposed a series of criteria to define patient response in the context of clinical trials of LDH. M-JOA scale is a modified edition of JOA Back Pain Evaluation Questionnaire. According to these criteria, a patient with LDH is assessed for pain, the ability to conduct daily life and work, functional impairment and particular clinical examinations. This scoring system has been previously validated. The degree of LDH severity was divided into three levels: mild (score, <0), moderate (10–20) and severe (>20).

Therapeutic effect was assessed by comparing baseline and final conditions reported by the patient. We also recorded adverse effects reported by patients during treatment. Outcome measures were assessed before treatment, after 7 and 14 days’ treatment, and 6 months after the last moxibustion session.

Statistical methods

Statistical analysis

Data were analysed on an intention-to-treat (ITT) basis including all randomised participants with at least one measurable outcome report. The statistician conducting the analyses remained blinded to treatment groups. All analyses were conducted using SAS statistical package program (V9.1.3; SAS, Cary, North Carolina, USA).

Baseline data

Baseline characteristics are shown as mean ± SD for continuous data. We conducted between-group comparisons of baseline data using the two-sample t test or Wilcoxon rank sum test for continuous data and χ² test or Fisher’s exact test for sex composition considering p < 0.05 as statistically significant.

Outcome data

Between-group analysis of M-JOA score was performed using an unpaired t test and the 95% CI of the difference between groups. If M-JOA scores did not have normal frequency distribution, the data were modified before testing, and if not normal after transformation, we used the non-parametric Wilcoxon rank sum test. To check
whether the data had normal distribution frequency, we used Shapiro-Wilk or W tests. For the ITT analysis we adopted the principle of last observation carried forward (LOCF).

All adverse events reported during the study were included in the case report forms; the incidence of adverse events was calculated.

Dropouts and missing data
Reasons for dropouts or missing data were explored descriptively. Missing data were replaced according to the principle of LOCF.

Follow-up data
The primary outcome was M-JOA score. The primary analysis compared the two groups at 2 weeks. A secondary analysis compared the two groups at 6 months to assess whether any differences between groups were maintained over time.

Data integrity
The integrity of trial data was monitored by regularly scrutinising data sheets for omissions and errors. Data were double entered and the source of any inconsistencies was explored and resolved.

Adverse events
We defined adverse events as unfavourable or unintended signs, symptoms, or disease occurring after treatment that were not necessarily related to the moxibustion intervention. In each visit, adverse events were reported by participants and examined by the practitioner.

Ethics
Written consent was obtained from each participant. This study was approved by all relevant local ethics review boards. Ethics Committee of the Affiliated Hospital of Jiangxi University of TCM approved this trial (code no. 200810).

RESULTS

Recruitment
Participants aged 18–65 years were recruited from outpatients and inpatients in the four study centres. A total of 306 persons underwent screening; of these, 96 met inclusion criteria and received allocated interventions (figure 2). Among the 210 excluded patients, 173 did not meet inclusion criteria, 25 refused to participate because they were wary of the treatment, 12 refused to be randomised because they wanted to be treated by moxibustion plus acupuncture (3 cases) or might go abroad before the end point (4 cases). Thus 96 patients were randomly assigned into 2 treatment groups by 30 investigators. During the follow-up visits, two patients dropped out of the study. In the experimental group, one patient left prior to study completion because of a fall injury. The M-JOA score at baseline was carried forward to all time points. All patients receiving the full course of treatment attended follow-up at 6 months. None of these patients dropped out of the study due to adverse events.

Baseline
At baseline, men and women were equally represented. Most (81%) patients were aged <60 years. Mean total M-JOA score at baseline of both groups showed no significant difference (p>0.05). All subordinate scores had similar tendency in accordance with the total score. Demographic and clinical features at baseline did not differ across the two treatment groups (table 1).

Assessor blinded
We ensured assessor blinding in this trial. Patients were informed not to tell outcome assessors the treatment they were received. The outcome assessor was not involved in treatment administration.

Outcome
After intervention the two groups showed a significant improvement from baseline, measured as difference in total M-JOA score after 1 week of starting treatment (table 2). Total M-JOA score was significantly lower in the individualised dose group at weeks 1 and 2 (p<0.05). The effect already shown in the first week was maintained ≤6 months after finishing treatment. Mean total M-JOA score of both groups reduced sharply at the first week then remained decreased to the end of 6 months (figure 3).

Moxibustion time in the experimental group
The moxibustion dose was individualised in the experimental group, not in the control group. The duration ranged between 22–58 min, with a mean moxibustion duration of 42.7±5.4 min. We used a linear correlation to measure the strength of a relationship between change in M-JOA score and stimulation duration in the test group. The Pearson coefficient r=0.003, showing a poor correlation between the two values.

Safety
No adverse events were reported for the 96 participants.

DISCUSSION
Patients in the two groups showed marked improvements in pain and function parameters for ≤6 months of follow-up. Significant differences in total M-JOA score were observed between the groups, also evident during the follow-up period. Our results suggest that an individualised sensitivity elimination dose of heat-sensitive moxibustion treatment showed superior long-term effects.

In our study, no unwanted side effects of heat-sensitive moxibustion were observed. Several large surveys have also provided evidence that indirect moxibustion is a relatively safe treatment.15–17
To the best of our knowledge, our study is the largest reported randomised, controlled trial that compared effectiveness of an individualised sensitivity elimination dose with a standardised dose in the treatment of patients with LDH. The studies published to date had certain methodological deficiencies in the description and application of the method chosen for randomisation, concealment of the treatment assignment scheme and homogeneity of comparator groups; moreover, heterogeneity of follow-up periods was high.\textsuperscript{10-12} Unlike most previous studies of moxibustion, our study required participating therapists to fulfil a number of rigorous standards with regard to their medical education and practical training in TCM. In addition, our study used central randomisation to ensure adequate concealment in group assignment. The evaluation of the results and the statistical analysis were both carried out in blinded fashion. High follow-up rates were another factor for quality assurance.

Figure 2  Study flow chart.
Nonetheless, our study had some limitations, including a lack of blinding to moxibustion. A blinded study of moxibustion is challenging to conduct because it is almost impossible to blind therapists to the treatments they were delivering. Theoretically, three factors may impact on moxibustion dose: intensity, area and time. The two former factors are constant as a result of the standard size of moxa stick used in practice. Hence time is the variable parameter and plays an important part in moxibustion dose. We wondered how long the optimum dose should be for heat-sensitive moxibustion. The simplest and most obvious method refers to a standard 15 min as recommended by the universal textbook. Other proposed methods consider flushing of skin in the local region as indication of optimum dose regimen. However, our team’s experimental evidence suggests that this regimen may not be superior. In this study, our results support the notion that individualised sensitivity elimination dose is likely to be optimal in heat-sensitive moxibustion.

The aim of our study was to explore the best dose of heat-sensitive moxibustion for the treatment of LDH. In summary, our results suggested that the effectiveness of individualised sensitivity elimination dose appears superior to standardised dose in the treatment of LDH. The application of only 15 min of moxibustion was insufficient to exert maximum clinical effects. A mean moxibustion dose of 42.70±5.40 min (range 22–58 min) was superior.

### Table 1: Baseline characteristics of patients with LDH

<table>
<thead>
<tr>
<th></th>
<th>Individualised group</th>
<th>Standardised group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>46.8±11.5</td>
<td>47.9±11.2</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum–maximum</td>
<td>18–58</td>
<td>28–67</td>
</tr>
<tr>
<td>&gt; 60, n (%)</td>
<td>8(16.7%)</td>
<td>10(20.8%)</td>
</tr>
<tr>
<td>Sex n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21(43.8%)</td>
<td>25(52.1%)</td>
</tr>
<tr>
<td>Female</td>
<td>27(56.3%)</td>
<td>23(47.9%)</td>
</tr>
<tr>
<td>Duration of low back pain n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 months</td>
<td>10(20.8%)</td>
<td>15(31.3%)</td>
</tr>
<tr>
<td>2–6 months</td>
<td>13(27.1%)</td>
<td>10(20.8%)</td>
</tr>
<tr>
<td>7–12 months</td>
<td>13(27.1%)</td>
<td>12(25.0%)</td>
</tr>
<tr>
<td>1–5 years</td>
<td>10(20.8%)</td>
<td>10(20.9%)</td>
</tr>
<tr>
<td>&gt; 5 years</td>
<td>2(4.2%)</td>
<td>1(2.1%)</td>
</tr>
<tr>
<td>BMI, mean (SD), kg/m²</td>
<td>22.1 (2.7)</td>
<td>23.5 (2.4)</td>
</tr>
<tr>
<td>BMI, minimum–maximum, kg/m²</td>
<td>14.6–30.1</td>
<td>16.0–27.1</td>
</tr>
<tr>
<td>M-JOA grade n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>32(66.7%)</td>
<td>30(62.5%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>16(33.3%)</td>
<td>18(37.5%)</td>
</tr>
</tbody>
</table>

BMI, body mass index; LDH, lumbar disc herniation, M-JOA, Modified Improvement Japanese Orthopaedic Association scale.

### Table 2: Comparison of M-JOA scores at week 1, end of treatment (week 2) and follow-up (month 6), together with between group statistical tests

<table>
<thead>
<tr>
<th>Variable</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Month 6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>t Test</td>
</tr>
<tr>
<td>Totals</td>
<td>9.5</td>
<td>3.9</td>
<td>2.0*</td>
</tr>
<tr>
<td>Individualised group</td>
<td>11.4</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>Standardised group</td>
<td>6.6</td>
<td>4.8</td>
<td>2.4*</td>
</tr>
<tr>
<td>Standardised group</td>
<td>9.0</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td>M-JOA score at baseline (SD)</td>
<td>1.3±0.8</td>
<td>1.2±0.9</td>
<td></td>
</tr>
<tr>
<td>Radiating pain score mean</td>
<td>1.7±0.8</td>
<td>1.9±0.9</td>
<td></td>
</tr>
<tr>
<td>Stoop and lift heavy things score mean</td>
<td>1.6±0.9</td>
<td>1.5±0.9</td>
<td></td>
</tr>
<tr>
<td>Walk distance/time score mean</td>
<td>1.6±0.9</td>
<td>1.5±0.9</td>
<td></td>
</tr>
<tr>
<td>Daily time in bed score mean</td>
<td>2.2±0.8</td>
<td>2.1±0.8</td>
<td></td>
</tr>
<tr>
<td>Ability to work score mean</td>
<td>1.3±1.1</td>
<td>1.4±1.0</td>
<td></td>
</tr>
</tbody>
</table>

* p<0.05.
** p<0.01.

M-JOA, Modified Improvement Japanese Orthopaedic Association scale.
Summary points

▸ Moxibustion can elicit de qi in certain locations in low back pain.
▸ This sensation can be abolished by prolonging the moxibustion.
▸ We found this more effective than standard duration of moxibustion.

Contributors  RC and MC obtained funding for the research project. JX, ZC and BZ drafted the protocol; JX wrote the final manuscript. ZC contributed to the research and made critical revisions. BZ was responsible for the statistical of the trial and wrote portions of the statistical methods, data handling and monitoring sections. All authors read and approved the final manuscript.

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Competing interests  The authors declare that they have no competing interests.

Patient consent  Obtained.

Ethics approval  Ethics Committee of the Affiliated Hospital of Jiangxi University of TCM.

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