Rheumatol Int (2012) 32:2969–2978
DOI 10.1007/s00296-012-2367-7

REVIEW ARTICLE

Moxibustion for the treatment of osteoarthritis: a systematic review and meta-analysis

Tae-Young Choi · Jiae Choi · Kun Hyung Kim · Myeong Soo Lee

Received: 5 September 2011 / Accepted: 11 March 2012 / Published online: 30 March 2012

Abstract The aim of this review was to summarise and critically evaluate the evidence from randomised clinical trials (RCTs) of moxibustion as a treatment for patients with osteoarthritis (OA). Twelve databases were searched from their inception through July 2011. RCTs were considered whether they assessed any type of clinical outcome from moxibustion therapy for patients with OA localised to any joints. Two reviewers independently performed the selection of studies, data abstraction and validations. The risk of bias was assessed using the Cochrane criteria. Eight RCTs met our inclusion criteria, and most of them had significant methodological weaknesses. Six RCTs tested the effects of moxibustion against conventional oral drug therapies in patients with knee OA (KOA). Meta-analysis showed favourable effects of moxibustion on the response rate ($n = 540$; RR, 1.09; 95 % CI 1.03–1.17; $P = 0.005$; heterogeneity: $\chi^2 = 5.48$, $P = 0.36$, $I^2 = 9$ %). Two RCTs tested the effects of moxibustion on response rate after 2 months. The meta-analysis failed to show favourable effects of moxibustion ($n = 180$; RR, 1.10; 95 % CI 0.97–1.24; $P = 0.13$; heterogeneity: $\chi^2 = 0.03$, $P = 0.87$, $I^2 = 0$ %). In conclusion, consistent results show that moxibustion may be effective in symptom management in patients with KOA. However, because of the number of eligible RCTs and the high risk of bias in the assessment of the available RCTs, the evidence supporting this conclusion is limited.

Keywords Moxibustion · Osteoarthritis · Systematic review · Meta-analysis · Complementary and alternative medicine

Introduction

Osteoarthritis (OA) is thought to be the most prevalent chronic joint disease, and the incidence of osteoarthritis is rising with population ageing and the obesity epidemic [1]. The main symptoms of OA are pain, stiffness, swelling, tenderness and reduced physical function as a result of joint degradation, including that of cartilage surfaces and subchondral bone [2, 3]. Loss of joint function as a result of OA is a major cause of work disability and reduced quality of life [4]. The Centres for Disease Control and Prevention (CDC) estimates that OA and related arthritic conditions cost the US economy nearly $81 billion per year in direct medical care costs with indirect expenses of approximately $47 billion, including lost wages and decreased production [4]. The average direct cost of treating OA is approximately 1,000–2,600 USD per year per patient [5, 6], and the total annual costs are approximately 5,700–9,880 USD [7, 8]. Approximately 5 and 10–11 % of adults 60 years of age or older suffer from OA of the hip [2] and knee [3], respectively. Treatment for OA aims to alleviate pain and improve function in order to mitigate the reduction in patient activity [1]. However, most treatments do not modify the natural history or progression of OA and thus

Electronic supplementary material The online version of this article (doi:10.1007/s00296-012-2367-7) contains supplementary material, which is available to authorized users.

T.-Y. Choi · J. Choi · M. S. Lee (✉)
Medical Research Division, Korea Institute of Oriental Medicine, Daejeon 305-811, South Korea
e-mail: drmslee@gmail.com; mslee@kiom.re.kr

K. H. Kim
Department of acupuncture and moxibustion, Korean Medicine Hospital, Pusan National University, Yangsan, South Korea

are not considered curative. Because there is no known cure for OA, the main therapeutic strategy is symptomatic. Treatment includes analgesics, nonsteroidal anti-inflammatory drugs (NSAIDS), COX-2 inhibitors, glucocorticoids, topical analgesics and cartilage protective agents (e.g. diacerein, glucosamine and chondroitin) [1–3].

Moxibustion is a traditional Oriental medicine that uses the heat generated by burning herbal preparations containing mugwort (*Artemisia vulgaris)* to stimulate acupuncture points. Moxibustion is composed of several herbal preparations, including mainly dried mugwort leaves. Mugwort is used in the practice of traditional Chinese medicine in a pulverised and aged form called moxa. Mugwort can have haemostatic, analgesic and desiccant effects and relieve abdominal pain as well as shorten blood clotting times (fry after more significant role carbon) [9, 10]. Moxa extract may be absorbed when placed on acupuncture points and may stimulate these points by increased heat. Cones of varying size and substance, such as fresh ginger, garlic, aconite cake and salt, can be used with moxibustion. The particular procedure of indirect moxibustion is as follows: place some herbal medicine on the acupuncture point and knead some moxa wool into the shape of a cone to be ignited and placed on the herbal medicine for moxibustion. The size of the moxa cone should vary according to the individual conditions. For people of strong constitution, large cones, the size of a broad bean may be used, and for those of weak constitution, moderately sized cones as big as a soybean or as small as wheat grain can be used. The combustion of one moxa cone is referred to as one zhuang. Proper moxibustion on an acupoint requires repetition of this process 3–7 times. The moxibustion process has been used to facilitate healing by stimulating the flow of qi and strengthening the blood. Moxibustion has frequently been promoted as a treatment for rheumatic conditions, including muscle strain, osteoarthritis, shoulder pain, neck and back pain, post-laminectomy pain, scar pain, inflammatory polyarthritis, fibromyalgia and rheumatoid arthritis [11].

There are two main types of moxibustion used in Chinese medicine: direct moxibustion and indirect moxibustion. Direct moxibustion is applied directly to the skin surface at the acupuncture point. The mugwort may either remain on the skin until it is completely combusted (which will usually lead to some level of scarring following the treatment) or the mugwort can be lit and then removed before the skin is burnt. In indirect moxibustion, a layer of various herbal medicines, such as ginger, garlic, salt and other materials, is placed between the moxa cone and the skin. The purpose of this technique is the absorption of the therapeutically active components of the herbal medicines into the skin in various conditions combined with heat stimulation by moxibustion. Also, a mugwort stick is lit and held close to the skin, or a needle is wrapped in mugwort, inserted in one of the points of pressure and ignited.

Two systematic reviews of moxibustion for pain or rheumatic conditions have been completed [12, 13]. One of these studies included two randomised clinical trials (RCTs) for OA that compared moxibustion with drug therapy [13]. This review suggested that moxibustion might be beneficial for pain control in patients with knee OA (KOA). Recently, another review was published in 2011 that was based on the same 2 RCTs for OA but also included 2 additional RCTs [12]. The second review also described some favourable effects of moxibustion in the treatment for KOA. However, both reviews are now outdated. Currently, no systematic review specifically addressing the efficacy of moxibustion for the treatment for osteoarthritis is available. Therefore, the aim of this article was to update, complete and critically evaluate the evidence from RCTs examining the efficacy of moxibustion as a method of treatment for patients with OA.

Methods

Data collection

The following databases were searched from their inception through July 2011: Medline, AMED, EMBASE, CINAHL, PsycInfo, The Cochrane Library 2011 (Issue 7) and the Chinese Medical Database (CNKI) as well as six Korean medical databases (Korean Studies Information, DBPIA, the Korean Institute of Science and Technology Information, KERIS, KoreaMed and the Korean National Assembly Library). The search strategies are shown in Supplement 1. Additionally, our own files and journals (Focus on Alternative and Complementary Therapies and Forschende Komplementarmedizin through June 2011) were manually searched. Hardcopies of all articles were obtained and read in full. No restrictions on years or publication status were imposed. We did not publish this protocol in advance.

Study selection

Types of studies

All prospective randomised clinical trials (RCTs) and quasi-RCTs were included in this systematic review. We excluded trials in which moxibustion was part of a complex intervention as well as case studies, case series, qualitative studies and uncontrolled trials. Trials that failed to provide detailed results were also excluded. Trials published in the form of dissertations and abstracts were included. No language restrictions were imposed.

Participants

We included studies that concerned patients with osteoarthritis in any joint. Studies that included a mixture of different rheumatic patients were included only if it was possible to extract the data concerning each patient population separately.

Types of intervention

Studies that used any type of moxibustion (direct or indirect) for treating OA in any of the peripheral joints were included. Studies were included if moxibustion was used as the sole intervention or as an adjunct therapy in conjunction with another standard treatment for OA. We also included trials if the control group received the same concomitant treatments as the moxibustion group. We included controls of no treatment, sham moxibustion or relevant standard therapies for OA, including conventional drug, exercise and rehabilitation therapies. Trials were excluded if they had designs that did not allow for an evaluation of the effectiveness of moxibustion (e.g. by using a treatment for unproven efficacy in the control group or a comparison of two different forms of moxibustion) or if they adopted comparisons between treatments or groups that were expected to have similar effects to moxibustion (e.g. acupuncture).

Types of outcome measures

The outcomes were presented in terms of scales that measured the level of pain, stiffness, response rate and standardised assessments of symptoms of OA, including the WOMAC scale.

Data extraction, quality and validation

Hard copies of all articles were obtained and read in full by two independent reviewers (TYC and KHK). The data from these articles were validated and abstracted according to pre-defined criteria that included author information, country of origin of the study, sample size, age of the participants, site and duration of the OA, experimental and control intervention regimens, main outcomes, associated adverse events and author conclusions (Table 1).

The risk of bias was assessed using the assessment tool for 'risk of bias' from the Cochrane Handbook for Systematic Reviews of Interventions [14]. The following characteristics were assessed: (1) method of randomisation, (2) allocation concealment, (3) blinding, (4) incomplete outcome measures and (5) selective outcome reporting. Our review used 'Low (L), Unclear (U) and High (H)' as keys for the judgments. The answer L indicated a low risk of bias, U indicated that the risk of bias was uncertain and the answer H indicated a high risk of bias [14]. Given that it is impossible to blind therapists to the use of moxibustion, we assessed patient and assessor blinding separately. For the Chinese literature, the two independent reviewers extracted and analysed the data. Disagreements were resolved by discussion between the two reviewers.

Quantitative data synthesis

Because there was no important clinical heterogeneity, we synthesised the results in a meta-analysis. The mean change in the outcome measures between the end of the final intervention (post-treatment) and the baseline was used to assess the differences between intervention and control groups. Standardised mean differences (SMDs) or weight mean difference (WMD) were used because the studies measured the outcomes on different scales (WOMAC and VAS) and on the same scale, respectively. SMDs or WMD and 95 % confidence intervals (CIs) were calculated using the Cochrane Collaboration software (Review Manager Version 5.0 for Windows; Copenhagen, The Nordic Cochrane Centre). For studies with insufficient information, we contacted the primary authors to acquire and verify data when possible. Summary estimates of the treatment effects were calculated using the random effects model to account for expected heterogeneity. Differences between the treatment and control groups were considered relevant in the context of this study. We therefore used the pre- and post-treatment means and SDs for each group and assumed a conservative within-subject pretest/post-test correlation of 0.5 to calculate the SDs of the change in each group using the methods in the Cochrane Handbook. For dichotomous outcomes, we calculated risk ratio (RR) for risk estimating. Cochrane's Q test and I^2 were used to assess statistical heterogeneity. We determined that there was considerable heterogeneity when the Cochrane's Q test result resulted in $P < 0.10$ and I^2 above 75 %. If a sufficient number of studies (at least 10) were available, we attempted to assess publication bias using a funnel plot or Egger's regression test, whereby effect estimates of the common outcome measures were plotted against the sample size [15, 16].

Results

Trial flow and study characteristics

The literature search revealed 251 articles of which 243 studies were excluded. The reasons for article exclusion during the selection process are described in Fig. 1. Key data regarding the 8 included RCTs are summarised in Table 1 [17–24]. A total of 720 participants were included in these trials. All of the RCTs originated in China, included patients with KOA, and used indirect moxibustion and a parallel

Table 1 Summary of the randomised clinical studies of moxibustion for osteoarthritis

First author (Year)	Sample size (M/F)	Diagnostic criteria	Intervention group (regimen)	Control group (regimen)	Main outcomes	Intergroup differences	Comments
Cheng (2008) [17]	120 (27/93)	ACR	(A) Moxa (1 session = n.r., once every 2 days, 10 times/session, rest for 10 days between sessions, total 2 sessions, $n = 60$)	(B) Drug therapy (oral: diclofenac sodium, 75 mg, 1/d, 15 days, $n = 60$)	Response rate	RR, 2.32[1.71,3.14], $P < 0.00001$	
					NRS (10-point Likert scale)	MD, −0.15[−0.46,0.16], NS	
					VRS (5-point Likert scale)	MD, 0.12[−0.03,0.27], NS	
Sun (2008) [18]	60/56 (80 knees) (23/33)	Guiding principles of clinical research on new drugs of traditional Chinese medicine	(A) Moxa (1 session = n.r., once daily, 5 times, rest for 1 or 2 days, 10 times/session, total 2 sessions, ($n = 41$ knees)	(B) Drug therapy (oral: diclofenac sodium, 75 mg, 1/d, 20 days, $n = 39$ knees)	Response rate	RR, 1.06[0.93,1.20], NS	
Yang (2008) [19]	64 (82 knees) (25/39)	Guiding principles of clinical research on new drugs of traditional Chinese medicine	(A) Moxa (1 session = n.r., once daily, 10 times/session, total 2 sessions, $n = 33$, 41 knees)	(B) Drug therapy (oral: diclofenac sodium, 75 mg, 1/d, 20 days, $n = 31$, 41 knees)	Response rate	RR, 1.03[0.90,1.17], NS	The author reported a significant difference between the 2 groups in response rate after 2 months
					Response rate (2-month follow-up)	RR, 1.09[0.92,1.29], NS	
Ren (2010) [20]	100 (37/63)	Guiding principles of clinical research on new drugs of traditional Chinese medicine	(A) Moxa (1 session = 30 min, once daily, 5 times/week, 1 month, total 1 session, $n = 50$, 84 knees)	(B) Drug therapy (oral: diclofenac sodium, 75 mg, 1/d, 20 days, $n = 50$, 80 knees)	Response rate	RR, 1.24[1.04,1.47], $P = 0.01$	
Zhou (2010) [21]	70 (98 knee) (27/43)	Guiding principles of clinical research on new drugs of traditional Chinese medicine	(A) Moxa (1 session = n.r., once daily, 10 times/session, total 2 sessions, $n = 35$, 50 knees)	(B) Drug therapy (oral: diclofenac sodium, 75 mg, 1/d, 20 days, $n = 35$, 48 knees)	Response rate	RR, 1.11[0.94,1.31], NS	The author reported favourable effects of moxibustion on response rate (70 % improvement)
					Response rate (2-month follow-up)	RR, 1.11[0.93,1.33], NS	
					Knee symptom and sign score	MD, −4.41 [−7.86, −0.96], $P = 0.01$	
					Knee symptom and sign score (2-month follow-up)	MD, −7.96 [−11.42, −4.50], $P < 0.00001$	
					NRS (10-point Likert scale)	MD, 0.22 [−0.38,0.82], NS	

Table 1 continued

First author (Year)	Sample size (M/F)	Diagnostic criteria	Intervention group (regimen)	Control group (regimen)	Main outcomes	Intergroup differences	Comments
Zhang (2011) [22]	60 (22/38)	ACR	(A) Moxa (1 session = 30 min, once daily, 7 times/session, total 6 session, $n = 30$)	(B) Drug therapy (celecoxib 200 mg, 1/d, 6 weeks, $n = 30$)	Response rate	RR, 0.96[0.78,1.19], NS	
Zhang (2009) [23]	60 (25/35)	n.r.	(A) Moxa (1 session = 20 min, once daily, 7 times/session, rest 1 day, total 2 sessions, $n = 30$)	(B) Drug therapy (topical: diclofenac diethylamine emulgel, 1 g, 1/d, 2 weeks, $n = 30$)	Response rate	RR, 1.04[0.82,1.32], NS	Sample size calculation
					Lequesne score	MD, −0.13[−1.65,1.39], NS	
He (2009) [24]	60 (31/29)	ACR	(A) Moxa (1 session = 5 min, once daily, 6 times/session, rest for 1 day between sessions, total 3 sessions, $n = 30$), plus (B)	(B) Drug therapy (oral: diclofenac sodium, 25 mg, 3/d, 20 days, $n = 30$)	Response rate	RR, 1.35[1.02,1.79], $P = 0.04$	

ACR American College of Rheumatology; *MD* mean difference; *n.r.* not reported; *NRS* numeric rating scale; *NS* not significant; *RR* risk ratio; *VRS* verbal rating scale

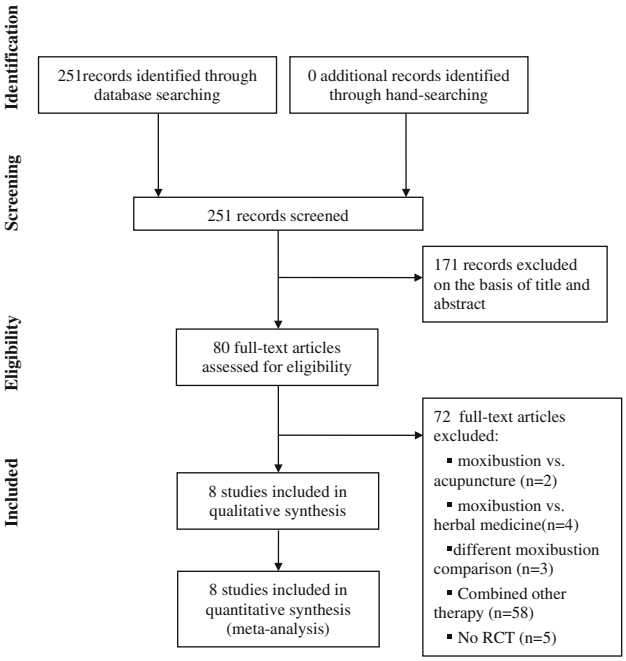

Fig. 1 Flowchart of the trial selection process. *RCT* randomised clinical trial

group design. Acupuncture point selection was based on traditional Chinese medicine (TCM) theory in all of the included RCTs. The details of the treatment regimens are summarised in Table 2 [17–24]. Five studies used cake-separated moxa [15–19], one used moxa stick [20], one used moderate moxa [21] and one used thin wood-separated moxa [22]. Three trials [17, 22, 24] used the KOA diagnosis criteria from the American College of Rheumatology, and four used the Guiding Principles of Clinical Research on New Drugs for TCM [18–21]. The remaining RCT did not describe the diagnostic methods employed [23].

Most trials had a relatively small sample size and a high risk of bias. Only three of the included trials employed appropriate sequence generation methods for randomisation [18, 21, 23] while the three other RCTs [17, 19, 24] used inappropriate methods (Table 3). The authors reported that they employed patient blinding in one RCT [17], while blinding procedures were unclear in the other 7 RCTs [18–24]. None adopted an allocation concealment method. The risk of bias for reporting participant dropout or withdrawal was low in one RCT [20]. None of the trials included an intention-to-treat analysis. Only one study calculated the appropriate sample size before performing the trial [23].

Quantitative data synthesis

Moxibustion versus conventional oral drug therapy

Six RCTs tested the effects of moxibustion compared with conventional oral drug therapies in patients with KOA

Table 2 Summary of the treatment points and other information related to the treatments

First author (Year)	Style of moxibustion	Treatment points	Rationales for selecting treatment points	Adverse events
Cheng (2008) [17]	Indirect (ginger, *panax notoginsengs* cake-separated moxa or aconite cake-separated moxa)	Fixed : EX-LE4, EX-LE5, EX-LE2, SP9, GB34 Individualised: Wind-cold obstructing the collaterals: GV14 Blood stasis due to qi stagnation: SP10 Liver–kidney deficiency: BL23	TCM theory	n.r.
Sun (2008) [18]	Indirect (aconite cake-separated moxa)	Individualised: EX-LE4, ST35, SP9, GB34, SP10, ST34, EX-LE2, BL18, BL23 in 2–4 points were chosen at every treatment	TCM theory	n.r.
Yang (2008) [19]	Indirect (*panax notoginsengs* cake-separated moxa)	Individualised: EX-LE5, EX-LE2, SP9, GB34, SP10, ST36 in 2–4 points were chosen at every treatment	TCM theory	n.r.
Ren (2010) [20]	Indirect (herbal cake-separated moxa containing musk, *olibanum, myrrh, clematis root, rhizoma chuanxiong, cinnamon, herba speranskiae tuberculatae,* etc.)	Individualised: EX-LE4, EX-LE5, ST34, SP10, ST35, SP9, GB34 in 4 points were chosen at every treatment	TCM theory	n.r.
Zhou (2010) [21]	Indirect (notoginseng cake-separated moxa)	Individualised: EX-LE4, EX-LE5, AShi-point, EX-LE2, SP9, GB34, SP10 and ST36 in 2–4 points were chosen at every treatment	TCM theory	n.r.
Zhang (2011) [22]	Indirect (moxa stick)	Fixed: SP10, ST34, BL40, GB34, etc.	TCM theory	(A): none; (B): 3 cases (n.r. in details)
Zhang (2009) [23]	Indirect (thin wood-separated moxa)	Fixed: EX-LE4, EX-LE5, GB33 and GV3	TCM theory	n.r.
He (2009) [24]	Indirect (thin wood-separated moxa)	Fixed: ST36, EX-LE4, EX-LE5	TCM theory	n.r.

TCM traditional Chinese medicine; *n.r.* not reported

[17–22]. Two of these studies reported superior effects of moxibustion on the response rate [17, 20] while the other four did not [18, 19, 21, 22]. The meta-analysis of the 6 eligible trials showed favourable effects of moxibustion on patient response rate ($n = 540$; RR, 1.09; 95 % CI 1.03–1.17; $P = 0.005$; heterogeneity: $\chi^2 = 5.48$, $P = 0.36$, $I^2 = 9$ %; Fig. 2a). Five studies compared the effects of moxibustion with those of oral diclofenac sodium (DS) treatment on patient response rates [17–21]. The meta-analysis also showed superior effects of moxibustion on the response rate when compared with oral DS ($n = 480$; RR, 1.11; 95 % CI 1.04–1.18; $P = 0.002$; heterogeneity: $\chi^2 = 4.04$, $P = 0.40$, $I^2 = 1$ %; Fig. 2a).

Two RCTs tested the effects of moxibustion on the response rate after 2 months [19, 21]. Although the authors of both of these studies claimed that moxibustion had a favourable effect on patient response rate, they failed to provide adequate evidence to support this conclusion (70 % symptom improvement compared with baseline). The meta-analysis also failed to show significantly different effects of moxibustion ($n = 180$; RR, 1.10; 95 % CI 0.97–1.24; $P = 0.13$; heterogeneity: $\chi^2 = 0.03$, $P = 0.87$, $I^2 = 0$ %; Fig. 2b).

Two RCTs compared the effects of moxibustion for pain on numeric rating scale with conventional drug therapy [17, 21], and both studies failed to show favourable effects of moxibustion ($n = 218$; WMD, 0.16; 95 % CI −0.11 to 0.44; $P = 0.24$; heterogeneity: $\chi^2 = 0.04$, $P = 0.84$, $I^2 = 0$ %; Fig. 2c).

One RCT [21] assessed knee symptoms and assigned scores according to the Guideline Principles of Clinical Research on New Drugs of TCM. Using this method, the authors showed significant improvement after treatment with moxibustion and at the 2-month follow-up period when compared with the control.

Moxibustion versus topical drug therapy

One RCT examined the effect of moxibustion on response rate and function using the Lequesne score. Using this

Table 3 Risk of bias in the included RCTs

Study	Random sequence generation	Allocation concealment	Patient blinding	Assessor blinding	Reporting dropout or withdrawal[a]	Intention-to-treat analysis[a]	Selective outcome reporting
Cheng (2008) [17]	H	U	L	U	U	U	U
Sun (2008) [18]	L	U	U	U	L	U	U
Yang (2008) [19]	H	U	U	U	U	U	U
Ren (2010) [20]	U	U	U	U	U	U	U
Zhou (2010) [21]	L	U	U	U	U	U	U
Zhang (2011) [22]	U	U	U	U	U	U	U
Zhang (2009) [23]	L	U	U	U	U	U	U
He (2009) [24]	H	U	U	U	U	U	U

Domains of quality assessment based on Cochrane tools for assessing risk of bias

L low risk of bias, *U* unclear risk of bias (uncertain risk of bias) and *H* high risk of bias

[a] Two domains referring to 'incomplete outcome data' in the Cochrane tools for assessing risk of bias

method, the authors failed to show the superiority of moxibustion for either outcome.

Moxibustion plus drug therapy versus drug therapy alone

One RCT [24] compared the effects of moxibustion in addition to drug therapy with drug therapy alone on the response rate of patients with KOA. The results showed favourable effects of moxibustion on the response rate.

Adverse effects

One RCT [22] assessed adverse effects while the other 7 RCTs did not. This study reported adverse events from drug therapy but failed to show the details.

Discussion

Overall, the trials included in this systematic review suggest that moxibustion may be an effective treatment for symptom management in patients with KOA. Whether the findings of beneficial effects compared with conventional drug therapy reflect equivalent effects is not yet clear. Furthermore, the risk of bias was high in all of the included trials. Hence, the evidence is not sufficient to conclude whether moxibustion was beneficial for treating the symptoms of KOA.

Our review aimed to update and complete the evidence by adding recent RCTs assessing moxibustion treatment in patients with KOA. Compared with the 2 previous reviews [12, 13], we identified 4 new RCTs [20–23] and successfully updated the available evidence concerning moxibustion therapy. The results of our review are similar to those reported in the other 2 reviews [12, 13]. One previous review [13] showed that moxibustion may be beneficial for symptom management in patients with any type of pain condition (including 2 studies on KOA), and the other review [12] also reported some favourable effects of moxibustion for rheumatic conditions (including 4 studies on KOA). Both reviews showed that moxibustion is effective for symptom management. However, these studies also expressed concerns regarding the poor methodological quality of the included primary studies.

According to the Cochrane criteria, the risk of bias was very high in all of the included studies. Inappropriate allocation concealment and a lack of blinding exaggerate the results of the outcome measures [25, 26]. The main limitations of the included studies were small sample sizes in most trials, inadequate controls for non-specific effects and a lack of power calculations or adequate follow-up. Additionally, the fact that moxibustion interventions cannot control for placebo effects limits the generalizability of the studies.

Although all of the included trials tested the effects of moxibustion compared with drug therapy, none tested the possible non-specific effects of moxibustion using appropriate sham controls. If we assume that the effects of moxibustion could result from stimulating acupuncture points with heat, then two possible controls could be derived. Sham moxibustion might include treating external acupuncture points on non-acupuncture points with moxa aroma without heat. Another option would be to prevent heat stimulation of acupuncture points or areas. Two sham moxibustion devices, which were designed to minimise heat transfer, were suggested [23, 27]. However, the main limitation of these methods is the lack of sensation at the acupuncture points. This limitation should be addressed in future possible placebo-controlled trials. One study compares moxibustion plus standard care versus standard care alone [24]. Assuming that moxibustion generates significant placebo effects, this type of study can only generate a positive result [28].

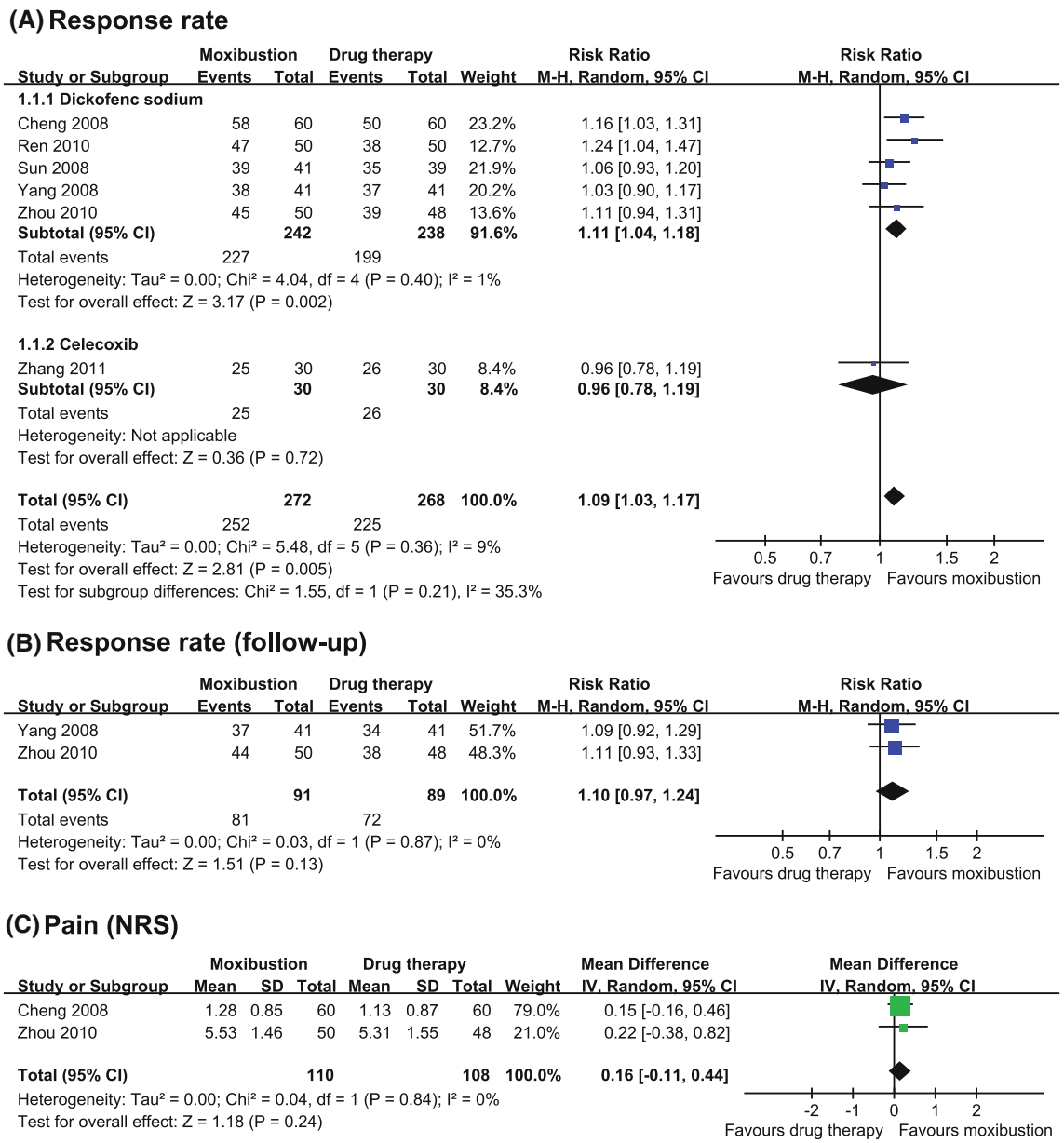

Fig. 2 Forest plot of the effects of moxibustion on **a** response rate, **b** response rate at the 2-month follow-up and **c** pain on a numeric rating scale (NRS; 10-point Likert scale) in patients with knee osteoarthritis

One of the included RCTs [22] reported adverse events. Adverse effects of moxibustion that have been reported in the literature include infections, burns and allergic reactions [29–31]. The possible occurrence of these adverse effects during moxibustion treatment should be monitored with caution.

One could argue that all of the included studies had a high risk of bias, thus causing this review to be meaningless and less informative. However, 'systematic reviews should identify and review all the relevant studies and are more likely to give a reliable answer. They use explicit methods and quality standards to reduce bias. Their results are the closest we are likely to get to the truth in the current state of knowledge, though much depends on how many clinical trials exist and how good and how large they are. Systematic reviews (and meta-analyses, the statistical combining of information from many trials) are our best defence against making incorrect decisions based on inadequate data' [32]. Additionally, this review provides readers the opportunity to access the primary studies published in China that they would otherwise be unable to read.

Acupuncture is an intervention that shares many characteristics with moxibustion. Therefore, it might be helpful

to consider the findings of a systematic review of acupuncture for the symptomatic treatment for peripheral KOA. A Cochrane systematic review identified 16 RCTs on acupuncture [33]. The authors concluded that 'sham-controlled trials show statistically significant benefits; however, these benefits are small and do not meet our predefined thresholds for clinical relevance'.

Culture-specific assessment and diagnosis of KOA might continue to be an issue in these studies. Four of the included RCTs used the Guideline Principles of Clinical Research on New Drugs of TCM [18–21]. Although these may be in accordance with the standard diagnostic criteria in conventional medicine, some discrepancies may continue to exist. Self-reported subjective questionnaires that are completed by patients, including the visual analogue scale and the WOMAC scale, are the most convenient method for collecting data regarding KOA. Only three of the RCTs used validated inventories for symptom or function improvement [17, 21, 23]. One of the included RCTs assessed knee symptoms and assigned scores using questionnaires that had not been tested for validity and reliability [21]. However, it seems important that only validated questionnaires be used in symptom management and assessment. Unless the reliability and validity of the outcome measures have been established, the data derived from the studies are subject to bias, and it is difficult to compare the results from different studies. All of the included studies used a response rate for each intervention, and the response rate was generally divided into one of the 4 following categories: (1) recovery, (2) marked improvement, (3) improvement and (4) no change. The patients were placed into these categories after assessment by the practitioners. This method is the most popular form of reporting efficacy rates, and it is similar to the global clinical improvements for intervention studies, including the assessment of conventional therapies. This method cannot avoid possible bias by the practitioner.

Only one of the reviewed studies reported minor adverse events related to moxibustion [22]. However, it is possible that moxibustion was directly responsible for the adverse events. There is one systematic review concerning adverse events of moxibustion [34]. This review showed that moxibustion is not entirely risk-free because it has several types of potential adverse events, including allergies, burns and infection. Therefore, adverse events should be examined in future studies.

Assuming that moxibustion is a beneficial treatment for rheumatic conditions, its mechanisms may be of interest. Moxibustion may allow for both absorption of moxa extract at the acupuncture points and direct acupuncture point stimulation from heat. Some aspects of the mechanisms of moxibustion may be similar those of acupuncture. Moxibustion effects may be mediated partially through opioidergic and/or monoaminergic neurotransmission [35, 36]. Another possible mechanism could involve the synergistic effects of heat from moxibustion on the stimulation of acupuncture points. Previous work suggests that moxibustion may modulate inflammatory reactions in an arthritis model [37]. In an arthritic rat model study, moxibustion improved the force of the rat's tread and alleviated nociceptive pain by regulating nitric oxide (NO) production and both c-Fos and nNOS expression [38]. None of these theories are, however, more than speculation at present.

The limitations of this study include the potential incompleteness of the reviewed evidence. The distorting effects of publication and location bias on systematic reviews and meta-analyses are well documented [39–41]. We are confident that our search strategy located all relevant data; however, some degree of uncertainty remains. Another possible source of bias is the fact that all of the included trials were performed in China, where no negative studies have been reported [42]. Our review may be affected by the potentially poor quality of the primary data and the poor reporting of results.

Future RCTs on the use of moxibustion for KOA should adhere to the accepted standards of trial methodology. The studies included in this review show a number of problems that have been noted by other meta-analyses examining the efficacy of moxibustion, such as the expertise of the practitioners, the frequency and duration of the treatment, the use of validated primary outcome measures and adequate statistical tests and the use of heterogeneous comparison groups. Furthermore, even though it is difficult to blind subjects to treatment, employing assessor blinding and allocation concealment are important for reducing bias.

In conclusion, consistent results show that moxibustion may be effective in symptom management in patients with KOA. However, because of the number of eligible RCTs and the high risk of bias among the available RCTs, the evidence supporting this conclusion is limited.

Acknowledgments TYC, JAC and MSL were supported by Korea Institute of Oriental Medicine (K10251 and K11111). The study sponsor had no involvement in study design; collection, analysis or interpretation of data; writing of the report; or in the decision to submit the paper for publication.

Conflict of interest The authors have no competing interests to declare.

References

1. Bijlsma JW, Berenbaum F, Lafeber FP (2011) Osteoarthritis: an update with relevance for clinical practice. Lancet 377:2115–2126
2. Scott D (2009) Osteoarthritis of the hip. Clin Evid 06:1122
3. Scott D, Kowalczyk A (2007) Osteoarthritis of the knee. Clin Evid 12:1121

4. Samson DJ, Grant MD, Ratko TA, Bonnell CJ, Ziegler KM, Aronson N (2007) Treatment of primary and secondary osteoarthritis of the knee. Evidence Report/Technology Assessments, No. 157. Available from http://www.ahrq.gov/downloads/pub/evidence/pdf/oaknee/oaknee.pdf
5. Andrews G, Simonella L, Lapsley H, Sanderson K, March L (2006) Evidence-based medicine is affordable: the cost-effectiveness of current compared with optimal treatment in rheumatoid and osteoarthritis. J Rheumatol 33:671–680
6. Rabenda V, Manette C, Lemmens R, Mariani AM, Struvay N, Reginster JY (2006) Direct and indirect costs attributable to osteoarthritis in active subjects. J Rheumatol 33:1152–1158
7. Gupta S, Hawker GA, Laporte A, Croxford R, Coyte PC (2005) The economic burden of disabling hip and knee osteoarthritis (OA) from the perspective of individuals living with this condition. Rheumatology (Oxford) 44:1531–1537
8. Maetzel A, Li LC, Pencharz J, Tomlinson G, Bombardier C (2004) The economic burden associated with osteoarthritis, rheumatoid arthritis, and hypertension: a comparative study. Ann Rheum Dis 63:395–401
9. Qu Y, Zeng R, Liu Y (2005) General situation of the studies of chinese mugwort (artemisia argyi) leaves. J Southwest Univ Nation (Natural Sci Edition) 31:254–256
10. Zhou YD, Fei XY (2010) Pharmacological studies on mugwort. Hubei J Tradit Chin Med 32:75–76
11. Camp AV (1998) Acupuncture for rheumatological problem. In: Filshie J, White A (eds) Medical acupuncture. Chuchil Livingston, Edinburgh, pp 801–804
12. Choi TY, Kim TH, Kang JW, Lee MS, Ernst E (2011) Moxibustion for rheumatic conditions: a systematic review and meta-analysis. Clin Rheumatol 30:937–945
13. Lee MS, Choi TY, Kang JW, Lee BJ, Ernst E (2010) Moxibustion for treating pain: a systematic review. Am J Chin Med 38: 829–838
14. Higgins JPT, Altman DG, Sterne JAC (2011) Chapter 8: assessing risk of bias in included studies. In: Higgins JPT, Green S (eds) Cochrane handbook for systematic reviews of interventions version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2008. Available from http://www.Chochrane-handbook.Org
15. Sterne JAC, Egger M, Moher D (2011) Chapter 10: addressing reporting biases. In: Julian PTH, Green S (eds) Cochrane handbook for systematic reviews of interventions version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2008. Available from http://www.Chochrane-handbook.Org
16. Borenstein M, Hedges LV, Higgins JPT, Rothestein HR (2009) Chapter 20: meta-regression. In: Borenstein M, Hedges LV, Higgins JPT, Rothestein HR (eds) Introduction to meta-analysis. Wiley, West Sussex, pp 187–204
17. Cheng HL, Han W, Hu PJ, Yang J (2008) Clinical study of differential selection of objects separated moxibustion for treatment of knee osteoarthritis. Clin J Tradit Chin Med 20:114–116
18. Sun K, Yang YH, Zhou ZL (2008) Clinical observations on the treatment of primary genual osteoarthritis of liver-kidney depletion type by aconite cake-separated moxibustion. Shanghai J Acup Moxi 27:9–10
19. Yang YH, Sun K, Su GH, Zhou CL (2008) Clinical study panax notoginsengs cake separated moxibustion treatment of qi stagnation blood stasis type for primary knee osteoarthritis. Clin J Tradit Chin Med 20:53–55
20. Ren XM, Song SL, Shi Y (2010) Observations on the therapeutic effect of herbal cake-separated moderate moxibustion on knee osteoarthritis of 50 cases. Zhejiang J Tradit Chin Med 45:759
21. Zhou ZL, Sun K, Cheng HL, Liu DC, Yang J (2010) Observations on the therapeutic effect of herbal cake-separated moxibustion on knee osteoarthritis of blood stasis type. Shanghai J Acup Moxi 29:45–47
22. Zhang QJ, Cao LH, Li ZD, Wang SC, Ma YH, Su JC, Zhang CC, Du N (2011) The clinical effects and safety of moxibustion and celecoxib for obteoarthritis of knee. Chin J Tradit Med Trauma Orthop 19:1315
23. Zhang S (2009) The clinical observation on the therapy of knee joint osteoarthritis using moderate moxibustion. MS thesis, Guangzhou University of Chinese Medicine
24. He Y, Xu YP, Huo XT (2009) Clinical research of moxibustion in treating knee joint osteoarthritis. Chin J Tradit Med Trauma Orthop 17:38–39
25. Pildal J, Hrobjartsson A, Jorgensen KJ, Hilden J, Altman DG, Gotzsche PC (2007) Impact of allocation concealment on conclusions drawn from meta-analyses of randomized trials. Int J Epidemiol 36:847–857
26. Schulz KF, Chalmers I, Hayes RJ, Altman DG (1995) Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. JAMA 273:408–412
27. Park JE, Lee MS, Choi SM (2009) Letter to the editor—Re: Is it possible to blind subjects using sham moxibustion treatment? Am J Chin Med 37:407–409
28. Ernst E, Lee MS (2008) A trial design that generates only ''positive'' results. J Postgrad Med 54:214–216
29. Park JE, Lee SS, Lee MS, Choi SM, Ernst E (2010) Adverse events of moxibustion: a systematic review. Complement Ther Med 18:215–223
30. White A, Hayhoe S, Hart A, Ernst E (2001) Survey of adverse events following acupuncture (SAFA): a prospective study of 32,000 consultations. Acupunct Med 19:84–92
31. White A, Hayhoe S, Hart A, Ernst E (2001) Adverse events following acupuncture: prospective survey of 32 000 consultations with doctors and physiotherapists. BMJ 323:485–486
32. Moor A, McQuay H (2006) Bandolier's little book of making sense of the medical evidence. Oxford University Press, Oxford
33. Manheimer E, Cheng K, Linde K, Lao L, Yoo J, Wieland S, van der Windt DA, Berman BM, Bouter LM (2010) Acupuncture for peripheral joint osteoarthritis. Cochrane Database Syst Rev. CD001977
34. Park JE, Lee SS, Lee MS, Choi SM, Ernst E (2010) Adverse events of moxibustion: a systematic review. Complement Ther Med 18:215–223
35. Han JS (2003) Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. Trends Neurosci 26:17–22
36. Han JS (2004) Acupuncture and endorphins. Neurosci Lett 361: 258–261
37. Wang T, Xie S (1990) Effect of moxibustion on the inflammatory reactions of adjuvant arthritics rats. Acupunct Res 15:44–47
38. Kim JH, Kim HK, Park YI, Shohnic IC, Choi DO, Kim MS, Park BR (2006) Moxibustion at ST36 alleviates pain in complete greund's adjuvant-induced arthritic rats. Am J Chin Med 34: 57–67
39. Egger M, Smith GD (1998) Bias in location and selection of studies. BMJ 316:61–66
40. Ernst E, Pittler MH (1997) Alternative therapy bias. Nature 385:480
41. Rothstein HR, Sutton AJ, Borenstein M (2005) Chapter 1: publication bias in meta-analysis. In: Rothstein HR, Sutton AJ, Borenstein M (eds) Publication bias in meta-analysis: prevention, assessment and adjustments. Wiley, Chichester
42. Vickers A, Goyal N, Harland R, Rees R (1998) Do certain countries produce only positive results? A systematic review of controlled trials. Control Clin Trials 19:159–166