

Meta-Analysis of the Clinical Efficacy of Taohong Siwu Decoction in the Treatment of Knee Osteoarthritis

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Abstract: *Objective:* To conduct a meta-analysis to systematically evaluate the clinical efficacy of Taohong Siwu Decoction in treating knee osteoarthritis (KOA) and to provide data for the clinical application of Taohong Siwu Decoction in the treatment of KOA. *Methods:* The five major databases of HowNet (CKNI), Wanfang, VIP, PubMed, and Chinese Biomedical Database (CBM) were used to search for relevant papers, the search time was from the establishment of the database to April 15, 2023. The relevant data were extracted from randomized controlled trials (RCT) of the treatment of KOA with modified Taohong Siwu Decoction that met the inclusion and exclusion criteria. The risk of bias was assessed using the Cochrane tool, and the data were imported into RevMan5.3 software for statistical analysis. *Results:* The search included 11 RCT literature involving 951 cases. Among them, there were 487 cases in the observation group (modified Taohong Siwu Decoction or modified Taohong Siwu Decoction + control group) and 464 cases in the control group (traditional Chinese medicine or conventional Western medicine). According to meta-analysis: (1) The effective rates of modified Taohong Siwu Decoction ($P = 0.03$) and modified Taohong Siwu Decoction + control group ($P < 0.0001$) in the treatment of KOA were significantly higher than that of the control group. (2) The VAS score of the observation group was significantly lower than the control group ($P < 0.00001$). (3) The Lysholm knee function score of the observation group was significantly higher than the control group ($P < 0.00001$). *Conclusion:* Compared with conventional Western medicine or simple traditional Chinese medicine, modified Taohong Siwu Decoction or its combination with conventional Western medicine or traditional Chinese medicine in treating KOA can improve the treatment effective rate and Lysholm knee function score, and reduce VAS score.

Keywords: Taohong Siwu Decoction; Knee osteoarthritis

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1. Introduction

Osteoarthritis of the knee is a common degenerative disease of articular cartilage, the risk of which increases with age. There are several clinical treatment options, but the main focus remains to relieve symptoms. With

the advanced development of traditional Chinese medicine research in recent years, the research on the pathogenesis of knee osteoarthritis (KOA) has also made significant progress^[1]. Non-surgical treatment is the first treatment option clinically for KOA, including traditional Chinese and Western medicine treatments. Taohong Siwu Decoction promotes blood circulation, removes blood stasis, and nourishes qi and blood^[2]. There are many literature reports on the treatment of KOA with Taohong Siwu Decoction, but the sample size of each literature is small and lacks credibility. Therefore, this study evaluates the clinical efficacy of Taohong Siwu Decoction in treating KOA by conducting a meta-analysis to provide an evidence-based basis for clinical practice^[3].

2. Material and methods

2.1. Inclusion and exclusion criteria

2.1.1. Inclusion criteria

- (1) Research type: Taohong Siwu Decoction was the leading research object in randomized controlled trials (RCT) limited to Chinese and English papers.
- (2) Research objects: The research objects were patients with knee osteoarthritis, which were diagnosed according to the diagnostic criteria of the American College of Rheumatology (ACR):
 - (i) Pain in the knee joint occurred within one month before seeing the doctor.
 - (ii) X-ray films showed bone spurs or hyperosteoegeny.
 - (iii) There was an abnormal friction sound when the knee joint moved.
 - (iv) Knee joint swelling, floating patella test (+).
 - (v) Aged over 40 years old.
 - (vi) Morning stiffness occurred for less than 30 minutes.The diagnosis can be made if one of the two diagnoses of (i), (ii) or (i), (iii), (iv), (v), (vi) is met. Race, gender, age, region, and other conditions are not limited.
- (3) Intervention measures: The control group was treated with conventional Western medicine or traditional Chinese medicine; the observation group was treated with modified Taohong Siwu Decoction alone, or Taohong Siwu Decoction combined with the primary treatment of the control group; when it comes to primary treatment, the two groups must be consistent.
- (4) Outcome indicators: The indicators included effective rate, visual analog scale (VAS) for pain score, and Lysholm knee function score.

2.1.2. Exclusion criteria

- (1) Article that does not belong to randomized controlled trials (RCT).
- (2) Article that belongs to non-randomized clinical trials such as experience, review, and individual cases.
- (3) The literature information is incomplete or has errors.
- (4) Duplicate publications.
- (5) Intervention measures do not meet the standards.
- (6) Non-Chinese and English papers^[4].

2.2. Data screening

The online databases such as CNKI (Chinese National Knowledge Infrastructure), CBM (China Biomedical Database), VIP, Wanfang Medical Journal Database, and PubMed were used to search for relevant papers and the search time was limited from the establishment of the database to April 15, 2023. After excluding

duplicative publications in each database, two researchers independently read and screened the literature according to the inclusion and exclusion criteria. Subsequently, the two researchers checked the literature. If there was any disagreement, a third researcher discussed whether to include it. The extracted content included first author, year of publication, sample size, intervention measures, outcome indicators, and Jadad score^[5].

2.3. Quality evaluation

Two researchers used the evaluation manual provided by the Cochrane Collaboration Network system and the Jadad scoring scale^[5] to evaluate the risk of bias in the included literature. The evaluation contents of the former include:

- (1) Random allocation: According to the different allocation methods, they are classified as low risk (such as lottery, random number table method) and high risk (such as grouping by admission order or admission date).
- (2) Allocation concealment.
- (3) Whether to choose blind method: It is divided into single-blind, double-blind, and triple-blind.
- (4) Completeness of result data.
- (5) Selective publication.
- (6) Other biases.

According to the standard, the researchers made judgments such as yes (low risk), no (high risk), and unclear for the above six items, expressed in the risk of bias map.

The Jadad scoring scale includes the following content:

- (1) Generation of random number sequence: 2 points for appropriate, 1 point for unclear, 0 point for inappropriate^[6].
- (2) Concealment of randomization: 2 points for appropriate, 1 point for unclear, 0 point for inappropriate and non-use.
- (3) Blinding: 2 points for appropriate, 1 point for unclear, and 0 point for inappropriate.
- (4) Withdrawal: 1 point for those with descriptions, 0 point for those without descriptions.

A Jadad score of 1–3 is considered low-quality research, 4–7 is regarded as high-quality research, and the total score is 7 points. After completing the evaluation, the two researchers compared the data. If there was any disagreement, it was discussed and decided by a third researcher^[7].

2.4. Statistical methods

The collected data were processed with RevMan5.3 software. The heterogeneity test was carried out on the included research results. If $P > 0.1$, $I^2 \leq 50\%$, there was homogeneity, and the fixed effects model was used to analyze it; if $P < 0.1$, $I^2 > 50\%$, there was heterogeneity that was analyzed using a random effects model. Binary variables were represented by odds ratio (OR) and its 95% confidence interval (CI). Continuous variables were defined by mean difference (MD) if the outcome data units were consistent. Otherwise, the standard deviation (SD) and its 95% CI were used.

3. Results

3.1. Literature search results

624 papers were obtained using the mentioned databases in the initial inspection. After eliminating 447 duplicate records, two researchers screened 177 RCT papers based on the titles and abstracts and then read the entire text of the 90 papers. According to the above exclusion criteria, 79 articles were excluded, and 11 were

finally included. In the included literature, there were 951 patients, including 487 cases in the observation group and 464 cases in the control group. The flow chart of the literature screening is shown in **Figure 1**.

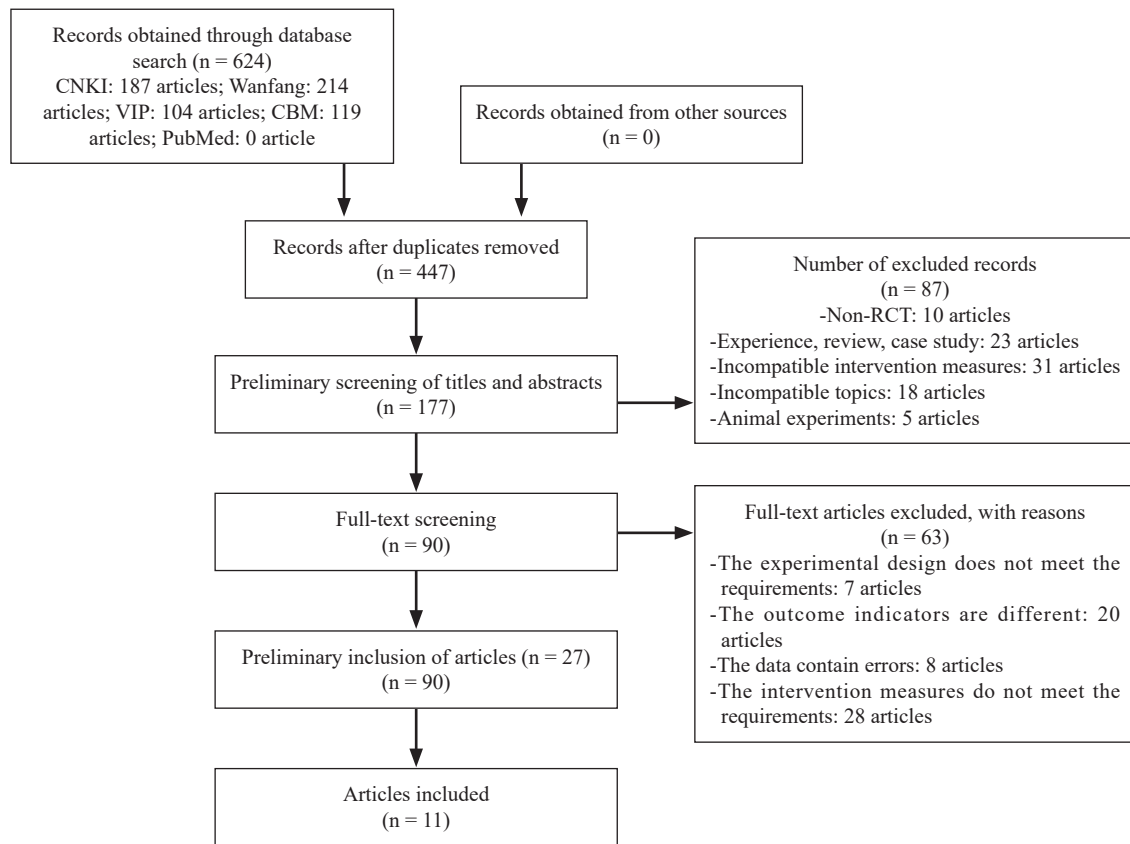


Figure 1. Flow chart of literature screening

3.2. Basic characteristics of the included literature

Among the 11 included literature, a total of 10 literature ^[4,6-14] conducted a comparative analysis of the effective rates of the two groups, five literature ^[7,8,11-13] compared and analyzed the VAS scores of the two groups, and three literature ^[7,8,15] compared the Lysholm knee function scores between the two groups. Among them, the outcome indicators of the VAS score reported in one article ^[11] did not meet the inclusion requirements, and only the effective outcome indicators were extracted. The essential characteristics of the included literature are shown in **Table 1**.

Table 1. Essential characteristics of the included literature

| First author | Year | Sample size (cases) | | Interventions | | Outcome indicators | Jadad score |
|--------------|------|---------------------|---------------|--|--|--|-------------|
| | | Observation group | Control group | Observation group | Control group | | |
| Wu Di | 2022 | 35 | 35 | Taohong Siwu Decoction | Western medicine treatment | Effectiveness rate | 1 |
| Fang Xiaolin | 2016 | 48 | 48 | Taohong Siwu Decoction + control group | Ozone | Effectiveness rate + VAS score + Lysholm knee function score | 2 |
| Xing Peng | 2021 | 40 | 40 | Taohong Siwu Decoction + control group | External application of traditional Chinese medicine + physiotherapy | Effectiveness rate + VAS score + Lysholm knee function score | 4 |

Table 1. (Continue)

| First author | Year | Sample size (cases) | | Interventions | | Outcome indicators | Jadad score |
|-----------------|------|---------------------|---------------|--|---|--------------------------------|-------------|
| | | Observation group | Control group | Observation group | Control group | | |
| Guo Zhanying | 2020 | 41 | 41 | Taohong Siwu Decoction | Physiotherapy | Effectiveness rate | 1 |
| Lu Na | 2018 | 51 | 49 | Taohong Siwu Decoction + control group | Warm acupuncture | Effectiveness rate | 1 |
| Wang Xiang-peng | 2015 | 70 | 50 | Taohong Siwu Decoction + control group | Warm acupuncture | Effectiveness rate | 2 |
| Zhao Wanliang | 2015 | 40 | 40 | Taohong Siwu Decoction | Glucosamine hydrochloride capsules | Effectiveness rate + VAS score | 3 |
| Qin Hong | 2013 | 52 | 52 | Taohong Siwu Decoction + control group | Rehabilitation training + traditional Chinese medicine fumigation | Effectiveness rate + VAS score | 1 |
| Liu Min | 2018 | 30 | 29 | Taohong Siwu Decoction | Mannitol | Effectiveness rate + VAS score | 2 |
| Zhu Lanfei | 2013 | 30 | 30 | Taohong Siwu Decoction | Basic treatment | Lysholm knee function score | 2 |
| Deng Yong | 2019 | 50 | 50 | Taohong Siwu Decoction | Ibuprofen | Effectiveness rate | 1 |

3.3. Methodological quality evaluation of included literature

The 11 included studies were all RCTs, four of which were grouped by random number table method, two by lottery method, and the remaining five did not specify the specific random method for grouping. Only one study explained allocation concealment. Four studies clarified that blinding was not used, the remaining seven did not mention the use of blinding, and four studies mentioned and explained case dropout. One of the studies had incomplete information, and the other 10 had complete baseline information. None of the 11 included studies reported selectively included literature [12]. There was one paper with modified Jadad score of 4 points indicating a high-quality study, and the scores of other literatures were all 1–3 points, which represented a low-quality study. The methodological quality evaluation of the included literature is shown in **Figures 2 and 3**.

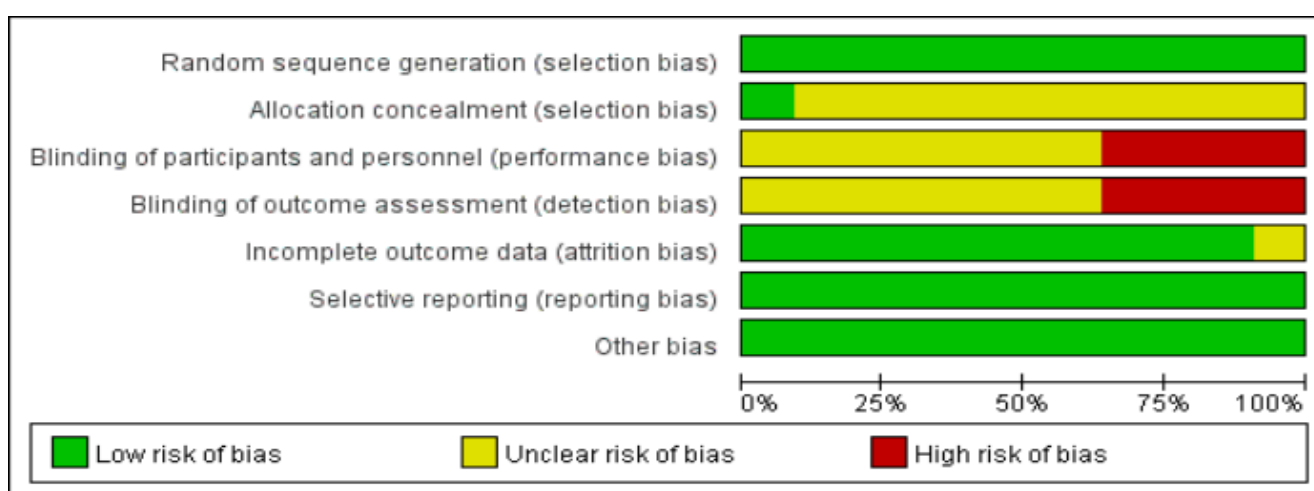


Figure 2. Risk of bias assessment

| Author (Year) | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|---------------|---|---|---|---|--|--------------------------------------|------------|
| 刘敏 2018 | + | ? | ? | ? | + | + | + |
| 吕娜 2018 | + | ? | - | - | + | + | + |
| 吴笛 2022 | + | ? | - | - | + | + | + |
| 方小林 2016 | + | ? | ? | ? | + | + | + |
| 朱兰妃 2013 | + | ? | ? | ? | + | + | + |
| 王象鹏 2015 | + | ? | ? | ? | + | + | + |
| 秦洪 2013 | + | ? | - | - | + | + | + |
| 赵万良 2015 | + | + | ? | ? | + | + | + |
| 邓勇 2019 | + | ? | ? | ? | ? | + | + |
| 开鹏 2021 | + | ? | ? | ? | + | + | + |
| 郭占英 2020 | + | ? | - | - | + | + | + |

Figure 3. Risk of bias summary

3.4. Meta-analysis results

3.4.1. Treatment effectiveness

The ten studies were subgroup-analyzed according to different intervention measures, among which the intervention measures of 5 studies were modified Taohong Siwu Decoction versus conventional treatment in control group. The heterogeneity test results revealed $P = 0.22$ and $I^2 = 30\%$, which shows that the homogeneity among the five studies was good, and the fixed effects model can be used. The calculated MD = 2.39, 95% CI [1.10, 5.19], $Z = 2.20$, $P < 0.03$, which shows that the difference in treatment effectiveness between the two groups is statistically significant, that is, the effective rate of modified Taohong Siwu Decoction in the treatment of KOA is significantly higher than that of conventional therapy alone. The intervention measures of the five studies were modified Taohong Siwu Decoction + control group versus control group. The heterogeneity test obtained $P < 0.0001$ and $I^2 = 0\%$, showing that the homogeneity among the five studies was good. The fixed effects model was used, obtaining MD = 4.29, 95% CI [2.18, 8.44], $Z = 4.22$, $P < 0.0001$, indicating that the difference in the effective rate of KOA treatment between the two groups was statistically significant. The differences among the subgroups were not statistically significant ($P = 0.47$, $I^2 = 0\%$), indicating that the subgroup factors were not the source of heterogeneity (Figure 4) [13].

3.4.2. VAS scores

Five studies reported VAS scores, and the heterogeneity test results showed $P < 0.00001$ and $I^2 = 96\%$, indicating heterogeneity among the studies, thus the random effects model was used for analysis. The results of the meta-analysis showed that compared with the control group, the VAS score of the observation group was significantly lower, [MD = -0.77, 95% CI (-0.87, -0.66), $P < 0.00001$], as shown in Figure 5 [15].

3.4.3. Lysholm knee function score

Three clinical trials reported Lysholm knee function score and heterogeneity test ($P = 0.10$, $I^2 = 57\%$). The results of the meta-analysis showed that compared with the control group, the knee joint function score of the observation group was significantly higher, [MD = 6.87, 95% CI (6.23, 7.52), $P < 0.0001$], as shown in Figure 6.

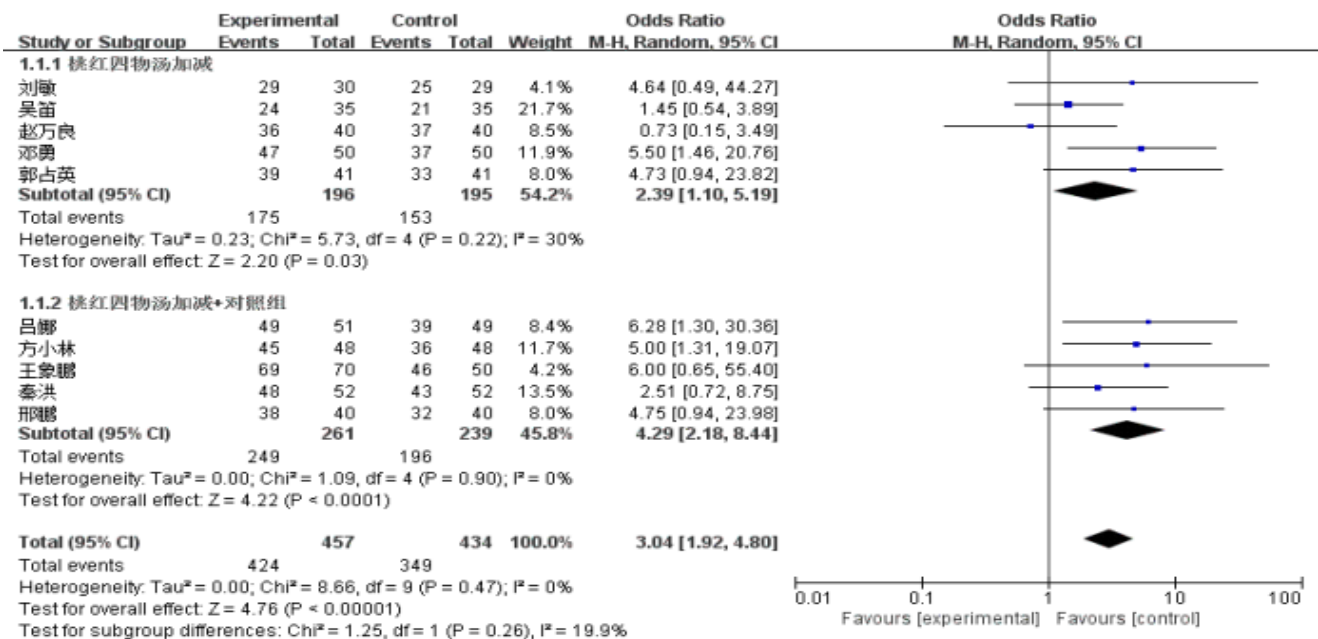


Figure 4. Forest plot of the effective rate of modified Taohong Siwu Decoction in the treatment of KOA

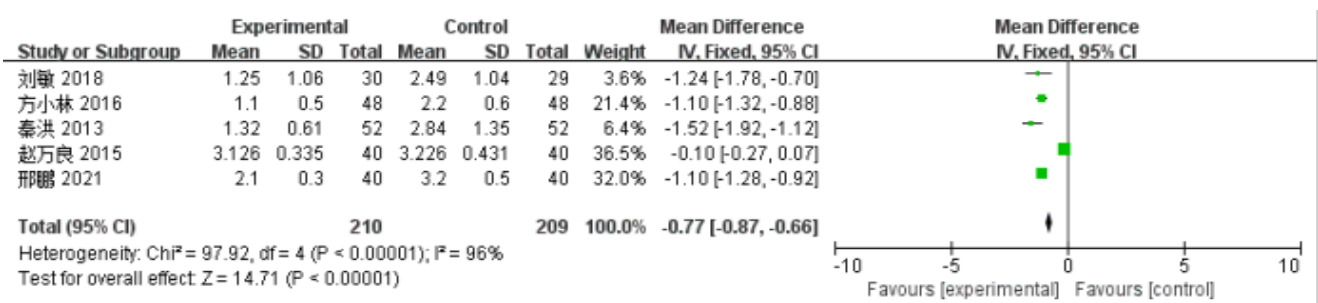


Figure 5. Forest plot of the VAS score of modified Taohong Siwu Decoction in the treatment of KOA

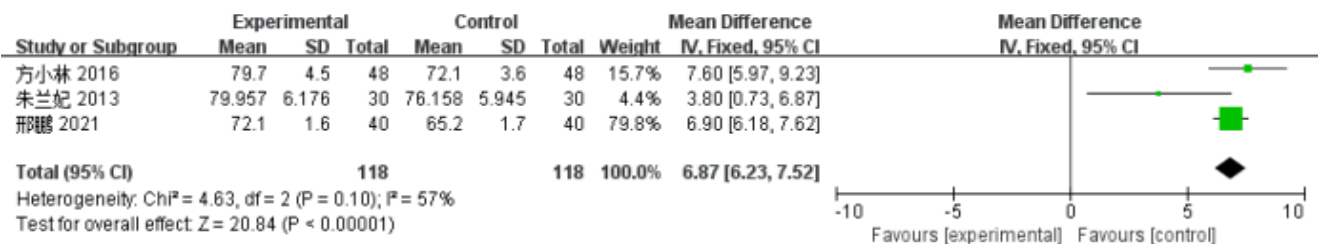


Figure 6. Forest plot of the knee joint function scores in the treatment of KOA with modified Taohong Siwu Decoction

4. Discussion

4.1. KOA in Chinese medicine

KOA is a prevalent clinical disease affecting older adults with persistent strain and knee inflammation. According to Chinese medical philosophy, KOA is classified as arthralgia and tendon injury related to old age, fatigue, and exogenous pathogenic factors. Taohong Siwu Decoction contains peach kernel, *Angelica sinensis*, red peony, Chuanxiong, myrrh, safflower, rhubarb, licorice, and other medicinal materials, which have the therapeutic effect of promoting blood circulation, removing blood stasis, and relieving pain. The formula is

adjusted according to the patient's condition to ensure the therapeutic effect. According to the results of this study, the modified Taohong Siwu Decoction was significantly better than the treatment used in the control group in terms of clinical treatment effect and knee function score, indicating that the drug has an excellent clinical curative effect in the treatment of knee osteoarthritis and can effectively relieve the clinical symptoms of patients. The main advantage of the decoction is that it can restore the function of the knee joint and improve the prognosis of patients, which is worthy of clinical application and promotion in the future.

4.2. Limitations

The following are the main limitations of this study:

- (1) The quality of the included studies is generally poor, there was no description of case drop-out and follow-up, some studies introduced the randomization procedure and allocation concealment inaccurately, and all studies did not explain the use of blinding.
- (2) The included studies have a significant degree of heterogeneity, which somewhat weakens the validity of the meta-analysis results.
- (3) Some studies did not state whether patients with other comorbidities should stop taking the drug, which may impact the research results.
- (4) This study only retrieved Chinese and English literature, so there may be omissions.

4.3. Future work

Taohong Siwu Decoction has a definite curative effect in treating KOA. It can effectively cure patients' clinical symptoms and has few side effects, so it is worthy of clinical promotion. To assist the development of various clinical studies in the future, we should pay more attention to the use of objective and standardized diagnostic criteria, avoid observations being affected by different drug additions and doses, improve the use of random methods, allocation concealment, and blinding procedures, in order to benefit various clinical research work in the future^[14].

Disclosure statement

The author declares no conflicts of interest.

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