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# The Chinese patent medicine Tongfengding capsule for gout in adults: a systematic review of safety and effectiveness

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## Abstract

**Background** Gout is a common inflammatory arthritis caused by increased serum uric acid levels. Untreated or insufficiently treated gout can lead to deposition of monosodium urate crystals in joints, cartilage, and kidneys. Although Tongfengding capsules, a Chinese patent medicine, have long been used to treat gout, their effects and safety have not been reviewed systematically. This study evaluated its efficacy and safety for gout in adults.

**Methods** Randomized controlled trials involving Tongfengding capsule for gout in adults were searched from PubMed, EMBASE, Cochrane Central Register of Controlled Trials, CBM, CNKI, and VIP databases, and analyzed using the Cochrane Handbook criteria. The primary outcome measures were the total effective rate. The secondary outcome measures including the blood uric acid (BUA), 24-h urinary total protein (24-h UTP), blood urea nitrogen (BUN), interleukin (IL)-6, IL-8, tumor necrosis factor-alpha (TNF-α) and adverse effects. The risk of bias was evaluated in all included studies. RevMan ver. 5.3.5 and GRADE profiler was used for data analysis and assessing the quality of evidence, respectively.

**Results** Six studies (n = 607 Chinese participants) were included. Tongfengding capsules plus conventional treatment significantly increased the total effective rate (RR 1.21, 95% CI 1.11–1.33), while reducing the BUA (MD − 66.05 μmol/L, 95% CI − 81.26 to − 50.84), 24-h UTP (MD − 0.83 g/24 h, 95% CI − 0.96 to − 0.70), BUN (MD − 0.90 mmol/L, 95% CI − 1.60 to − 0.20), IL-6 (MD − 6.99 ng/L, 95% CI − 13.22 to − 0.75), IL-8 (MD − 12.17 ng/L, 95% CI − 18.07 to − 6.27), TNF-α (MD − 8.50 ng/L, 95% CI − 15.50 to − 1.51), and adverse effects (RR 0.21, 95% CI 0.04–0.95).

**Conclusion** Tongfengding capsules plus conventional treatment is safe and beneficial for adults with gout compared with conventional treatment.

**Keywords** Chinese patent medicine, Tongfengding capsule, Gout, Randomized controlled trials, Systematic review

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## Introduction

Gout is a common type of inflammatory arthritis caused by increased serum levels of uric acid (UA) that exceed the limit of solubility of 7.0 mg/dL, leading to the deposition of monosodium urate crystals in joints, cartilage, and tissues [1–3]. Its main clinical features including tophi deposition, specific recurring acute arthritis, chronic gouty arthritis, and deformed joints [4–6]. Gout usually affects the kidneys, causing the formation of urinary tract stones and chronic interstitial nephritis composed of UA [4, 7]. Gout caused by hyperuricemia is associated with rapid deterioration of renal function in patients with chronic kidney disease [3, 8]. The prevalence of gout is 3.9% in the US, affecting 8.3 million adults [9–12], 2.5% in the UK [13], and 5.2% in Australia [14]. In China, it is more commonly seen in the population over the age of 40 years [4]. Epidemiological evidence suggests that gout is becoming more prevalent over time [15, 16]. Acute gout causes short-term disability, which led to an average of five additional work days off each year and an estimated increase in medical care costs of US$3165 annually per affected person [17]. Untreated or insufficiently treated gout can lead to chronic manifestations of the disease, such as persistent inflammation, the development of tophi, and joint damage [18–20].

The management of an acute gout includes treatment with colchicine, non-steroidal anti-inflammatory drugs (NSAIDs), adrenocorticotrophic hormones, and steroids. Uricosuric and diuretic drugs are used to prevent rebound gout in patients without kidney damage or a history of kidney stones [16]. The standard Western medicine therapy for the disease focuses on the therapy of the primary disease such as high UA levels [4]. Clinical guidelines recommend colchicine and NSAIDs as first-line therapy to treat acute gout [4, 21]. Corticosteroids are a potential first-line treatment to decrease joint inflammation in acute gout [4, 22, 23]. However, many studies have reported that colchicine and NSAIDs increase the risk for gastrointestinal tract bleeding and reactions in the short term as well as cardiovascular adverse events in the longer term [24–26]. NSAIDs are contraindicated in patients with renal or liver dysfunction, bleeding disorders, and heart failure, hindering the use of these drugs in patients at higher risk for recurrent acute gout [27]. Studies reported that corticosteroids have fewer clinical contraindications and drug side effects, particularly in people with chronic kidney disease [27, 28]. Although uricosuric drugs, allopurinol, and diuretic drugs are used to prevent rebound gout in patients without kidney impairment or a history of kidney stones [16, 29, 30], the potential of cardiovascular and gastrointestinal risks are well documented. Besides, patients with gastritis/ulcers, hypertension, congestive heart failure, or kidney insufficiency who suffer from gout have a high risk of side effects when taking the above drugs [16, 31, 32]. Therefore, it is not surprising why patients with gout seek complementary and alternative therapies.

On the basis of the traditional Chinese medicine (TCM) theory, gout is an "impediment disease" (*bi zheng*: a group of diseases caused by the invasion of wind, dampness, cold, or heat pathogens on the meridian/channel involving sinews, muscles, bones, and joints, manifest by soreness, heaviness, local pain, or hotness, and even articular swelling, deformities and stiffness, also referred to as arthralgia). TCM theory holds that "stagnation leads to pain." In TCM, the cause of gout involves dampness–heat and blood stasis pathogenic factors. In China, Chinese herbal medicine decoctions have a long history of being used to treat gout and have unique clinical effects [4]. In recent decades, an increasing number of studies have compared Chinese herbal medicine decoctions and traditional Western medicine for the therapy of gout. But, there are some disparities in the therapy methods and effect among these studies [33], which affects the replicability and reliability of the conclusions and makes it difficult to appreciate the findings [34].

Tongfengding capsules, a Chinese patent medicine, has long been used to treat gout. The capsules clear heat and eliminate dampness (*qing re chu shi*: a therapeutic method of treating dampness–heat in the middle and upper energizers by the combined use of heat-clearing and dampness-resolving medicinals), and activate blood to alleviate pain (*huo xue zhi tong*: a therapeutic method for treating painful conditions caused by blood stasis). Nevertheless, its effects and safety for the treatment of gout in adults have not been systematically reviewed. Therefore, this study was carried out to evaluate the efficacy and safety of Tongfengding capsule for treating gout in adults.

## Methods

### Criteria for included studies

#### *Inclusion criteria*

Type of studies: Only randomized controlled trials (RCTs) were included.

Types of participants: The selected studies included participants diagnosed with gout [35] who were ≥18 years of age, of either sex, and had not received corticosteroids or nonsteroidal anti-inflammatory drugs (NSAIDs) within 24 h of disease onset before randomization.

The diagnostic criteria for gout in all studies included hyperuricemia, more than one attack of acute arthritis, joint redness, painful or swollen first metatarsophalangeal joint, unilateral attack involving the tarsal joint, asymmetric swelling within a joint on radiograph,

subcritical cysts without erosions on radiograph, and/or joint fluid culture negative for organisms during an attack.

#### *Exclusion criteria*

Studies were excluded if the patients had accompanying debilitating conditions such as severe heart disease and liver or kidney failure, pregnant, or patients with joint deformities.

#### *Types of interventions*

The interventions included the Chinese patent medicine, Tongfengding capsules alone versus no treatment, placebo, or conventional treatment (e.g., colchicines, NSAIDs, other urate-lowering drugs, or/and symptomatic treatment); Tongfengding capsules plus conventional treatment versus placebo plus conventional treatment; and Tongfengding capsules plus conventional treatment versus conventional treatment.

The China Food and Drug Administration assesses Chinese patent medicines according to a strict drug evaluation process.

#### *Outcome measures*

The primary outcome measures included all-cause mortality and total effective rate (*cure*: total absence of the signs and symptoms of gout, including redness, swelling, heat, and joint pain, and erythrocyte sedimentation rate [ESR], blood uric acid [BUA], and C-reactive protein [CRP] levels in the normal range; *markedly effective:* substantially improved [≥ 50%] signs and symptoms including redness, swelling, heat, and joint pain, and reduced ESR, BUA and CRP levels, but remaining above normal range; *effective*: partially improved [≥ 30%] signs and symptoms including redness, swelling, heat, and joint pain with lower ESR, BUA, and CRP levels, but remaining above the normal range).

The secondary outcome measures included BUA, CRP, ESR, interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor alpha (TNF-α), serum creatinine (SCr), blood urea nitrogen (BUN), and 24-h urinary total protein (24-h UTP) levels, relapse rate, traditional Chinese medicine (TCM) tongue and pulse assessment (tongue coating and pulse), economic index, withdrawal, and adverse effects.

### Search methods used to identify studies

The following electronic databases and series of associative terms were searched, and all searches were completed on May 31, 2019: the Cochrane Central Register of Controlled Trials (to May 2019), Embase (1967–May 2019), PubMed (1966–May 2019), the Chinese National Knowledge Internet (1979–May 2019), the Chinese Biomedicine Database (1978–May 2019), and the VIP Chinese Science and Technology Periodical Database (1989–May 2019). The included trials were assessed using the Cochrane Handbook criteria [36].

We used the following search terms for the review: (traditional Chinese and Western medicine OR integrated Chinese and Western medicine OR Chinese medicine OR traditional Chinese medicine OR traditional Chinese pharmacy OR Chinese patent medicine OR Chinese patent drugs OR Chinese traditional patent medicine OR Chinese traditional herb OR Chinese medicinal herb OR Chinese herbal medicine OR Tongfengding capsule OR Tong-Feng-Ding-Jiao-Nang) AND (gout OR pain paralysis OR hyperuricemia OR Bi Zheng). We manually investigated the Journal of Guangzhou University of Traditional Chinese Medicine. We attempted to contact all of the original authors to clarify the protocols for each study.

### Data collection and analysis

#### *Study selection*

Two authors (QH and XL) independently browsed the titles and abstracts of all of the papers identified in the literature search. We assessed the abstracts retrieved in the initial search independently to identify studies that met the inclusion criteria. Uncertainties were resolved by consultation or discussion with a third author (QY). who independently determined whether the studies met the inclusion criteria. In this review, we telephoned the original authors of the trials to confirm the randomization procedure and other methodological procedures to ensure that only RCTs were included in our analysis. Studies were excluded if the inclusion criteria were not met.

#### *Data extraction and management*

We extracted the data using a pretested data extraction form and according to the study characteristics including methods, participants, interventions, and outcomes. No disagreements arose among the authors. We extracted the Chinese patent medicine content from the included studies, and the names of the Chinese herbal medicines are shown in Chinese, Latin, and English in Table 1.

#### *Assessment of risk of bias in the included studies*

We used a risk of bias assessment tool to assess the following items [36]: sequence generation (selection bias), allocation concealment (selection bias), blinding of the intervention allocations (including participants, personnel, and outcome assessors), handling of incomplete outcome data (attrition bias), alternative outcome reporting (reporting bias), and other potential biases.

**Table 1** Contents of the Chinese patent medicine (in three languages) used in the included studies

| Study ID | Herbs (composition) in three languages | Administration methods |
|---|---|---|
| Tang [40] | Tongfengding capsules (national drug approval number Z10970025, Sichuan Shenghe Pharmaceutical Co., Ltd.): Huangbai (*Cortex Phellodendri*/amur cork-tree bark), Qinjiao (*Radix Gentianae Macrophyllae*/large leaf gentian root or straw-colored gentian root), Chishao (*Radix Paeoniae Rubra*/red peony root) | Oral administration |
| Gao et al. [41] | Tongfengding capsules (national drug approval number Z10970025, Sichuan Shenghe Pharmaceutical Co., Ltd.): Huangbai (*Cortex Phellodendri*/amur cork-tree bark), Qinjiao (*Radix Gentianae Macrophyllae*/large leaf gentian root or straw-colored gentian root), Chishao (*Radix Paeoniae Rubra*/red peony root) | Oral administration |
| Chi and Li [42] | Tongfengding capsules (national drug approval number Z10970025, Sichuan Shenghe Pharmaceutical Co., Ltd.): Huangbai (*Cortex Phellodendri*/amur cork-tree bark), Qinjiao (*Radix Gentianae Macrophyllae*/large leaf gentian root or straw-colored gentian root), Chishao (*Radix Paeoniae Rubra*/red peony root) | Oral administration |
| Tang [43] | Tongfengding capsules (national drug approval number Z10970025, Sichuan Shenghe Pharmaceutical Co., Ltd.): Huangbai (*Cortex Phellodendri*/amur cork-tree bark), Qinjiao (*Radix Gentianae Macrophyllae*/large leaf gentian root or straw-colored gentian root), Chishao (*Radix Paeoniae Rubra*/red peony root) | Oral administration |
| Ao [44] | Tongfengding capsules (national drug approval number Z10970025, Sichuan Shenghe Pharmaceutical Co., Ltd.): Huangbai (*Cortex Phellodendri*/amur cork-tree bark), Qinjiao (*Radix Gentianae Macrophyllae*/large leaf gentian root or straw-colored gentian root), Chishao (*Radix Paeoniae Rubra*/red peony root) | Oral administration |
| Wang et al. [45] | Tongfengding capsules (national drug approval number Z10970025 Sichuan Shenghe Pharmaceutical Co., Ltd.): Huangbai (*Cortex Phellodendri*/amur cork-tree bark), Qinjiao (*Radix Gentianae Macrophyllae*/large leaf gentian root or straw-colored gentian root), Chishao (*Radix Paeoniae Rubra*/red peony root) | Oral administration |

#### *Assessment of treatment effect*

All statistical analyses were performed using the Cochrane Collaboration RevMan software ver. 5.3.5. Dichotomous (all-cause mortality, total effective rate, relapse rate, and adverse effects) and continuous (BUA, CRP, erythrocyte ESR, IL-6, IL-8, 24-h UTP, SCr, BUN, and TNF-α levels) variables were assessed. The data are expressed as risk ratios (RR) and 95% confidence intervals (CI).

The quality of evidence was assessed using GRADE profiler [37]. GRADE was divided into four levels of evidence: high, moderate, low, and very low [38].

#### *Dealing with missing data*

If necessary, the original authors were contacted by telephone to obtain required information. We carefully assessed all of the data, including screened and randomized participants as well as the as-treated, intention-to-treat, and per-protocol populations. Additionally, attrition rates (including losses to follow-up, dropouts, and withdrawals) were assessed. Problems that arose due to missing data and the attributed methods used were critically evaluated [36]. The original authors were contacted by telephone to clarify missing information. The primary authors of the included studies were contacted by telephone to obtain missing information.

#### *Assessment of heterogeneity*

Heterogeneity was assessed using the chi-squared test with n − 1 degrees of freedom and an alpha of 0.05 for statistical significance, and with the $I^2$ test values of 25%, 50%, and 75% corresponding to low, medium, and high levels of heterogeneity, respectively [39].

#### *Assessment of reporting biases*

We planned to use a funnel plot to assess reporting bias.

#### *Data synthesis*

We used a random effects model under the hypothesis that the effects being evaluative were not identical throughout, but followed certain assignment patterns, and a fixed-effects model to assure the stability of the model susceptibility and choice of outliers with a pooled data analysis of the included studies.

#### *Subgroup analyses*

Subgroup analyses were performed according to Tongfengding capsules and relieve pain drugs types (e.g., colchicines, indomethacin, or NSAIDs).

#### *Sensitivity analysis*

The sensitivity analysis was performed by excluding low-quality studies (based on allocation concealment, randomization, double-blinded or blinded assessment of outcomes, and analyses/descriptions of dropouts and withdrawals) followed by comparisons of the pooled data from the random- and fixed-effects models.

## Results

### Search results

Our search strategy identified 217 records, one of which was in an English language database. After removing 51 duplicates, 166 papers were included initially, 153 of which were subsequently excluded because they did not meet the inclusion criteria (not an RCT, n = 41; animal studies, n = 37; wrong intervention, n = 23; and wrong disease, n = 52). Of the 13 potentially eligible studies,

six were excluded from further assessment; in one of these, the comparator was a Chinese herbal medicine that lacked sufficient evidence of effect, two studies assessed the wrong intervention, the exclusion criteria were unclear in two studies, and the remaining study had unclear inclusion and exclusion criteria. The missing information in one study could not be obtained and it is awaiting assessment. Therefore, our review includes six studies (607 Chinese participants; Fig. 1).

## Included studies

### *Participants*

Six studies [40–45] were included comprising 607 adults with gout. The trial populations were small, ranging from 64 to 180 Chinese participants (average: 101.17 participants). All of the studies were conducted in China. The ratio of male to female participants in five of the trials was 345/180 [40, 41, 43–45]. Participant ages ranged from 30 to 87 years. The disease duration was not reported in two of the studies [40, 42]. In total, 607 adults with gout were included in six studies, and all of the participants were from China.

### *Interventions*

The primary intervention was oral administration of the Chinese patent medicine Tongfengding capsule. The therapy duration ranged from 7 days to 12 weeks. The follow-up duration was 6 months in two studies [41, 45], three studies mentioned follow-up but did not specify the duration [42–44], and the remaining study did not mention follow-up [40]. All six studies compared Tongfengding capsule plus conventional treatment versus conventional treatment alone. NSAIDs, urate-lowering drugs, and symptomatic treatment were the main conventional treatments for gout in adults. The medication used in these studies including NSAIDs (diclofenac

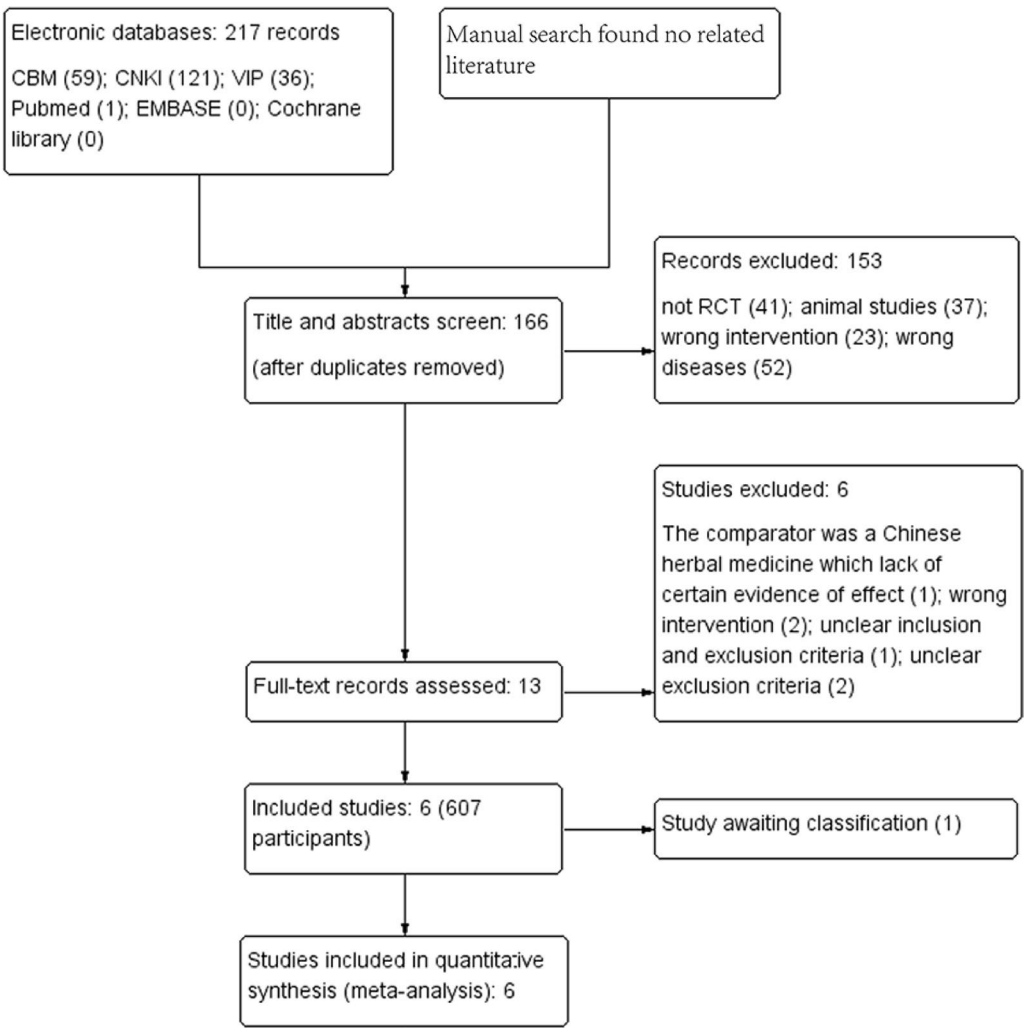


**Fig. 1** Summary of the search results in a flow diagram

sodium dual release enteric-coated capsules [44] and diclofenac sodium enteric-coated sustained release capsules + indomethacin [45]), xanthine oxidase inhibitor (allopurinol [40] and Febuxostat tablets [43]), xanthine oxidase inhibitor (Benzbromarone capsules) + indomethacin [41], and colchicine + xanthine oxidase inhibitor (allopurinol) [42].

#### *Outcomes*

The total effective rate was reported in four studies [41–44], BUA concentration was reported in four studies [40, 41, 43, 45], CRP and ESR were reported in one study [40], Il-6, Il-8, and TNF-α levels were reported in two studies [40, 43], 24-h UTP was reported in one study [40]; SCr and BUN were reported in one study [43]; the relapse rate and adverse effects were reported in two studies [41, 45], and the withdrawal rate was reported in one study [42]. However, none of the studies reported all-cause mortality, economic index, or TCM tongue and pulse assessment (tongue coating and pulse). The characteristics of the included studies are shown in Table 2.

### Risk of bias in the included studies

The methodological quality of each study, including the randomization sequence, allocation concealment, blinding (blinding of the personnel and participants and blinding of the outcome assessment), incomplete outcome data, selective outcome reporting, and other bias is shown in Figs. 2 and 3.

#### *Randomization and allocation concealment*

All six included studies [40–45] reported that the patients were randomized; however, only four provided sequencing details [40–42, 45], all of which used a random number table to assign groups [40–42, 45]. We conducted telephone interviews with the authors of the remaining two studies and found that one used a computer-generated random sampling table [44] and the other used a random number [43]. Although none of the six studies [40–45] reported their allocation concealment methods, we concluded that the concealment procedures were sufficient because the investigators were not actively involved in treatment, and the physicians treating the participants were unaware of the study outcome parameters.

#### *Blinding*

Three studies [43–45] reported using double blinding (neither the participants nor investigators were aware of the drug allocation) and single blinding (participants were not aware of the outcome assessment), but did not describe their procedures. We interviewed the original authors by telephone to clarify their blinding procedures and concluded that the studies had low risks of performance and detection biases. In contrast, the risks of performance and detection biases in the three studies [40–42] that did not mentioned blinding procedures are unclear.

#### *Incomplete outcome data*

The outcome data were clearly reported in the included studies [40–45], which showed no withdrawals, dropouts, and/or loss to follow-up. However, the methods used to handle missing data (i.e., per-protocol analysis or intention-to-treat) were not described.

#### *Selective reporting*

Although none of the six included studies [40–45] provided detailed evidence of selective reporting, the published papers included all of the expected outcomes, including those that were pre-specified. Funnel plot was not performed due to small sample size.

#### *Other potential sources of bias*

The participant demographic characteristics were comparable among the six included studies. Four studies mentioned that their institutional ethics committees approved the protocol and that written informed consent was obtained from each participant [40–42, 45]. We confirmed ethics committee approval and written informed consent in the remaining two studies [43, 44] in telephone interviews with the authors.

### Excluded studies

We excluded six studies from our review. Of these, one was excluded because the comparator was a Chinese herbal medicine that did not have sufficient evidence of efficacy; two were excluded because they used the wrong intervention; one was excluded because the inclusion and exclusion criteria were not clear; and the remaining two studies were excluded due to unclear exclusion criteria.

### Studies awaiting classification

One potentially eligible study is awaiting assessment because the information provided is not adequate to determine whether it meets the inclusion criteria for our review, and we have been unable to contact the original authors directly.

### Effects of interventions

#### *Primary outcome*

*Total effective rate* Four studies [41–44] reported that Tongfengding capsules plus conventional treatment significantly increased total effective rate when compared to conventional treatment [Fig. 4; Analysis 1.1; RR 1.21, 95% CI 1.11–1.33; $I^2 = 0\%$].

**Table 2** Characteristics of the included studies

| | |
|---|---|
| Tang [40] | |
| Methods | Randomized controlled trial (RCT): randomization described in detail<br>Allocation concealment: not mentioned; however, the randomization method would have prevented participants/investigators from knowing or influencing the treatment group before eligible participants were enrolled in the study<br>Follow-up: not mentioned<br>Study duration: 30 days<br>Parallel/factorial/crossover RCT: parallel RCT<br>Randomization method: a random number table was used<br>Blinding: no details were provided<br>Intention to treat (ITT): not mentioned |
| Participants | Setting: Chinese patients of hospital, but did not mention if inpatients or outpatients<br>Country: China<br>Number (randomized/analyzed): Treatment group (90/90); control group (90/90)<br>Treatment group: 52 males (57.8%) and 38 females (42.2%), age 30–35 (43.7 ± 4.6) years, disease duration: not mentioned<br>Control group: 54 males (60%) and 36 females (40%), age 30–55 (42.9 ± 4.8) years, disease duration: not mentioned |
| Interventions | Treatment group: Chinese patent medicine Tongfengding capsules plus conventional treatment<br>Tongfengding capsules containing Huangbai, Qinjiao, and Chishao; the Chinese medicine dose was not mentioned. Tongfengding capsules: three capsules orally taken three times daily (tid) for 30 days<br>Conventional treatment was the same as that used in the control group<br>Control group: conventional treatment: Allopurinol tablets (50 mg) orally taken twice daily (bid), extra water, low purine foods, and alcohol consumption prohibited for 30 days |
| Outcomes | 1. BUA<br>2.CRP<br>3. ESR<br>4. Il-6, Il-8, and TNF-α<br>5. 24-h UTP |
| Notes | 3. Economic index: not mentioned<br>4. TCM tongue and pulse assessment (tongue coating and pulse): not mentioned<br>5. Adverse effects (rash, diarrhea, and gastrointestinal discomfort): not mentioned<br>5. Source of funding: Project support, Project Number: Sichuan Technological Innovation Funding Project, 2015GF01299<br>6. Relapse rate: not mentioned<br>7. Withdrawals: not mentioned; however, the full text suggested that there were no withdrawals<br>8. The study was approved by the ethics committee and participants provided informed consent<br>9. Overall, the participant demographic data were similar between groups |
| Gao et al. [41] | |
| Methods | Randomized controlled trial (RCT): randomization described in detail<br>Allocation concealment: not mentioned; however, the randomization method would have prevented participants/investigators from knowing or influencing the treatment group before eligible participants were enrolled in the study<br>Follow-up: 6 months<br>Study duration: 4 weeks<br>Parallel/crossover/factorial RCT: parallel RCT<br>Randomization method: a random number table was used<br>Blinding: no details were provided<br>Intention to treat (ITT): not mentioned |
| Participants | Setting: outpatients<br>Country: China<br>Number (randomized/analyzed): Treatment group (41/41); control group (40/40)<br>Treatment group: 38 males (92.7%) and 3 females (7.3%), age 41.6 ± 2.8 years, disease duration: 7.8 ± 5.2 years<br>Control group: 38 males (95%) and 2 females (5%), age 40.2 ± 2.7 years, disease duration: 7.6 ± 6.4 years |
| Interventions | Treatment group: Tongfengding capsules plus conventional treatment<br>Tongfengding capsules containing Huangbai, Qinjiao, and Chishao, the dose was not mentioned. Tongfengding capsules four capsules orally tid for 4 weeks<br>Conventional treatment was the same as that used in the control group<br>Control group: conventional treatment: benzbromarone capsules, 50 mg orally once daily (qd), taken after breakfast; sodium bicarbonate tablets and dipyridamole tablets 0.5 g orally tid; Indomethacin tablets 25 mg orally tid, continuously for 3 days; a high purine diet was prohibited during the study period |
| Outcomes | 1. Total effective rate<br>2. BUA<br>3. Relapse rate<br>4. Adverse effects (rash, diarrhea, and gastrointestinal discomfort) |

**Table 2** (continued)

| | |
|---|---|
| Notes | 1. All-cause mortality: not mentioned<br>2. CRP: not mentioned<br>3. ESR: not mentioned<br>4. Il-6, Il-8, and TNF-α: not mentioned<br>5. Economic index: not mentioned<br>6. TCM tongue and pulse assessment (tongue coating and pulse): not mentioned<br>7.Source of funding: not mentioned<br>9. Withdrawals: not mentioned; however, the full text suggested that there were no withdrawals<br>10. The study was approved by the ethics committee and participants provided informed consent<br>11. Overall, the participant demographic data were similar between groups |
| Chi and Li [42] | |
| Methods | RCT: randomization described in detail<br>Allocation concealment: not mentioned; however, the randomization method would have prevented participants/investigators from knowing or influencing the treatment group before eligible participant were enrolled in the study<br>Follow-up: follow-up was mentioned; however, the follow-up duration was not mentioned<br>Study duration: 7 days<br>Parallel/crossover/factorial RCT: parallel RCT<br>Randomization method: a random number table was used in the study<br>Blinding: not mentioned<br>ITT: not mentioned |
| Participants | Setting: outpatients and inpatients<br>Country: China<br>Number (randomized/analyzed): treatment group (44/44); control group (38/38)<br>Treatment group and control group: the ratio of male to female and disease duration: not mentioned |
| Interventions | Treatment group: Chinese patent medicine Tong-Feng-Ding-Jiao-Nang capsules plus conventional treatment<br>Tongfengding capsules containing Huangbai, Qinjiao, Chishao; the Chinese medicine dose was not mentioned. Tong-Feng-Ding-Jiao-Nang capsules: 3–4 capsules orally tid for 7 days<br>Conventional treatment was the same as that used in the control group<br>Control group: conventional treatment included colchicine tablets 3 mg orally at first, then 0.5 mg every 1–2 h until the symptoms subsided or adverse effects occurred, with the stipulation of no more than 6 mg per 24 h, and 0.5 to 1 mg per day after 72 h; allopurinol tablets 0.1 g orally bid or tid |
| Outcomes | 1. Total effective rate<br>2. SCr<br>3. BUN |
| Notes | 1. BUA: not mentioned<br>2. Relapse rate: not mentioned<br>3. Adverse effects (rash, diarrhea, and gastrointestinal discomfort): not mentioned<br>4. All-cause mortality: not mentioned<br>5. CRP: not mentioned<br>6. ESR: not mentioned<br>7. Il-6, Il-8, and TNF-α: not mentioned<br>8. Economic index: not mentioned<br>9. TCM tongue and pulse assessment (tongue coating and pulse): not mentioned<br>10. Withdrawals: not mentioned; however, the full text suggested that there were no withdrawals<br>11. Source of funding: not mentioned<br>12. The study was approved by the ethics committee and participants provided informed consent<br>13. Overall, the participant demographic data were similar between groups |
| Tang [43] | |
| Methods | RCT: randomization mentioned, but not described in detail<br>Allocation concealment: not mentioned in the paper; however, allocation concealment was confirmed in a telephone interview with the author<br>Follow-up: not mentioned<br>Study duration: 3 months<br>Parallel/crossover/factorial RCT: parallel RCT<br>Randomization method: random number table use was confirmed via telephone interview<br>Blinding: double-blinding was confirmed via telephone interview<br>ITT: not mentioned |
| Participants | Setting: Chinese patients of hospital, but did not mention if inpatients or outpatients<br>Country: China<br>Number (randomized/analyzed): treatment group (40/40); control group (40/40)<br>Treatment group: 22 males (55%) and 18 females (45%), age 26–68 (45.6 ± 8.2) years, disease duration: 2–14 (6.3 ± 2.1) years<br>Control group: 24 males (60%) and 16 females (40%), age 23–67 (44.8 ± 7.8) years, disease duration: 1–12 (6.1 ± 1.8) years |

**Table 2** (continued)

| | |
|---|---|
| Interventions | Treatment group: Chinese patent medicine Tongfengding capsules plus conventional treatment<br>Tongfengding capsules containing Huangbai, Qinjiao, Chishao; the Chinese medicine dose was not mentioned. Tongfengding capsules 4 capsules orally tid for 3 months<br>Conventional treatment was the same as that used in the control group<br>Control group: conventional treatment included febuxostat tablets 80 mg orally qd for 3 months |
| Outcomes | 1. Total effective rate<br>2. Il-6, Il-8, and TNF-α<br>3. BUA |
| Notes | 1. Relapse rate: not mentioned<br>2. Adverse effects (rash, diarrhea, and gastrointestinal discomfort): not mentioned<br>3. All-cause mortality: not mentioned<br>4. CRP: not mentioned<br>5. ESR: not mentioned<br>6. Economic index: not mentioned<br>Economic index: not mentioned<br>7. TCM tongue and pulse assessment (tongue coating and pulse): not mentioned<br>8. Source of funding: not mentioned<br>9. Withdrawals: not specifically mentioned; however, careful reading of the paper confirmed that no participants withdrew from the study<br>10. Ethics committee approval and signed informed consent were not mentioned in the paper, but were confirmed in a telephone interview<br>11. Overall, the participant demographic data were similar between groups |
| Ao [44] | |
| Methods | RCT: randomization was mentioned, but not described in detail<br>Allocation concealment: not mentioned; however, the use of allocation concealment was confirmed in a telephone interview with the original author<br>Follow-up: not mentioned<br>Study duration: 3 months<br>Parallel/factorial/crossover RCT: parallel RCT<br>Randomization method: not mentioned; however, a telephone interview with the original author confirmed that a computer was used to generate random sequences<br>Blinding: not mentioned; however, a telephone interview with the original author confirmed the use of double-blinding<br>ITT: not mentioned |
| Participants | Setting: outpatients<br>Country: China<br>Number (randomized/analyzed): treatment group (32/32); control group (32/32)<br>Treatment group: 32 (19 males; 59.4%; 13 females; 40.6%), age 61–85 years (75.2 ± 1.2) years, disease duration: 6 months -5 (2.6 ± 0.2) years<br>Control group: 32 (20 males; 62.5%; 12 females; 37.5%), age 63–87 (75.5 ± 1.5) years, disease duration: 7 months -5 (2.8 ± 0.2) years |
| Interventions | Treatment group: Chinese patent medicine Tongfengding capsules plus conventional treatment<br>Tongfengding capsules containing Huangbai, Qinjiao, and Chishao, the Chinese medicine dose was not mentioned. Tongfengding capsules 4 capsules orally tid for 8 weeks<br>Conventional treatment was the same as that used in the control group<br>Control group: conventional treatment included diclofenac sodium double-release enteric capsules, 75 mg orally qd for 8 weeks |
| Outcomes | 1. Total effective rate |
| Notes | 1. Il-6, Il-8, and TNF-α: not mentioned<br>2. BUA: not mentioned<br>3. Relapse rate: not mentioned<br>4. Adverse effects (rash, diarrhea, and gastrointestinal discomfort): not mentioned<br>5. All-cause mortality: not mentioned<br>6. CRP: not mentioned<br>7. ESR: not mentioned<br>8. Economic index: not mentioned<br>9. TCM tongue and pulse assessment (tongue coating and pulse): not mentioned<br>10. Source of funding: not mentioned<br>11. Withdrawals: not specifically mentioned; however, careful reading of the paper confirmed that no participants withdrew from the study<br>12. Ethics committee approval and signed informed consent were not mentioned in the paper, but were confirmed in a telephone interview<br>13. Overall, the participant demographic data were similar between groups |

**Table 2** (continued)

| | |
|---|---|
| Wang et al. [45] | |
| Methods | RCT: random sequences were generated using a random number table<br>Allocation concealment: allocation concealment was confirmed in a telephone interview<br>Follow-up: 6 months<br>Study duration: 4 weeks<br>Parallel/factorial/crossover RCT: parallel RCT<br>Randomization method: random number table<br>Blinding: double-blinding was confirmed in a telephone interview<br>ITT: not mentioned |
| Participants | Setting: outpatients<br>Country: China<br>Number (randomized/analyzed): treatment group (60/60); control group (60/60)<br>Treatment group: 60 (38 males; 63.33%; 22 females; 36.67%), age 45.6 ± 5.7 years, disease duration: 6.8 ± 3.4 years<br>Control group: 60 (40 males; 66.67%; 20 females; 33.33%), age 46.7 ± 5.3 years, disease duration: 6.5 ± 2.8 years |
| Interventions | Treatment group: Chinese patent medicine Tongfengding capsule plus conventional treatment<br>Tongfengding capsules including Huangbai, Qinjiao, and Chishao; the Chinese medicine dose was not mentioned. Tongfengding capsules 4 capsules orally tid for 4 weeks<br>Conventional treatment was the same as that used in the control group<br>Control group: conventional treatment included anti-infection, low purine diet, diclofenac sodium enteric-coated sustained-release capsules 0.1 g orally qid, and indomethacin (dose not mentioned) orally during the acute phase of gout |
| Outcomes | 1. BUA<br>2. Relapse rate |
| Notes | 6. Economic index: not mentioned<br>7. TCM tongue and pulse assessment (tongue coating and pulse): not mentioned<br>8. Source of funding: not mentioned<br>9. Withdrawals: not specifically mentioned; however, careful reading of the paper confirmed that no participants withdrew from the study<br>10. Ethics committee approval and signed informed consent were not mentioned in the paper, but were confirmed in a telephone interview<br>11. Overall, the participant demographic data were similar between groups |

RCTs-randomized controlled trials; ITT—intention-to-treat; cholesterol; ESR—erythrocyte sedimentation rate; BUA—blood uric acid; CRP—C-reactive protein; IL-6—interleukin-6; IL-8—interleukin-8; TNF-α—tumor necrosis factor-α; Scr—Serum creatinine; BUN—Blood urea nitrogen; 24-h UTP—24-h urinary total protein

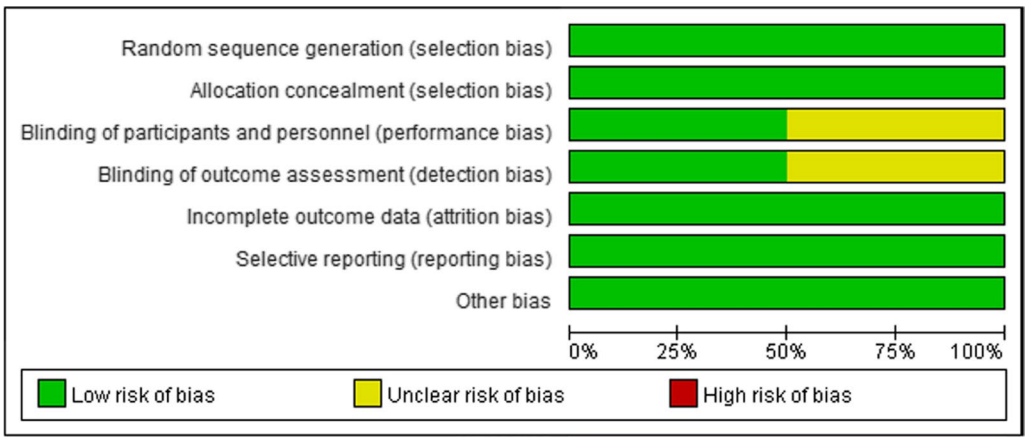


**Fig. 2** Risk of bias graph

### *Secondary outcomes*

*BUA* A significant decrease in BUA was observed with Tongfengding capsules plus conventional treatment versus conventional treatment [Fig. 5; Analysis 1.2; MD −66.05 μm/L, 95% CI −81.26 to −50.84; $I^2$ = 90%].

Three subgroup studies [40, 41, 43] reported that Tongfengding capsules plus urate-lowering drugs combined with relieve pain drugs significantly decreased BUA when compared to urate-lowering drugs combined with relieve

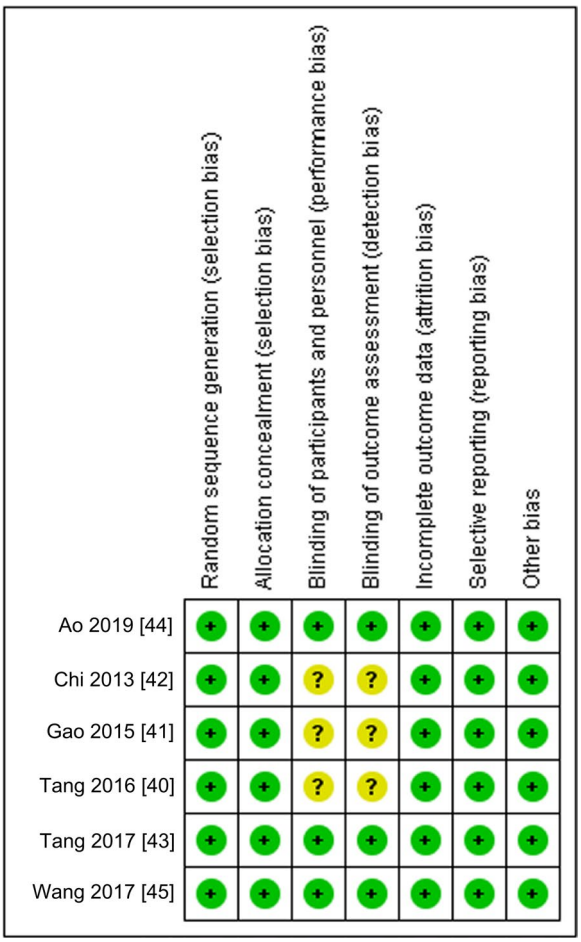


**Fig. 3** Methodology quality summary

pain drugs [Fig. 5; Analysis 1.2.1; MD −80.35 μm/L, 95% CI −83.04 to −77.66; $I^2$ = 0%].

One subgroup study [45] reported that Tongfengding capsules plus NSAIDs significantly decreased BUA when compared to NSAIDs [Fig. 5; Analysis 1.2.2; MD −28.95 μm/L, 95% CI −47.19 to −10.71].

*Kidney function (24-h UTP, SCr, and BUN)* One study [40] reported that Tongfengding capsules plus conventional treatment (allopurinol) significantly decreased 24-h UTP and BUN when compared to conventional treatment [Fig. 6; Analysis 1.3.1; MD −0.83 g/24 h, 95% CI −0.96 to −0.70] and [Fig. 6; Analysis 1.3.3; MD −0.90 mmol/L, 95% CI −1.60 to −0.20], respectively. In contrast, the study [40] showed that Tongfengding capsules plus conventional treatment did not significantly decrease SCr when compared against conventional treatment [Fig. 6; Analysis 1.3.2; MD −4.02 μm/L, 95% CI −8.18 to 0.14].

*Inflammatory factor (Il-6, Il-8, and TNF-α)* Two studies [40, 43] reported that Tongfengding capsules plus conventional treatment (allopurinol [40] and Febuxostat [43]) significantly decreased Il-6, Il-8, and TNF-α when compared to conventional treatment [Fig. 7; Analysis 1.4.1; MD −6.99 ng/L, 95% CI −13.22 to −0.75; $I^2$ = 96%], [Fig. 7; Analysis 1.4.2; MD −12.17 ng/L, 95% CI −18.07 to −6.27; $I^2$ = 93%], and [Fig. 7; Analysis 1.4.3; MD −8.50 ng/L, 95% CI −15.50 to −1.51; $I^2$ = 97%], respectively.

*Related indicators (CRP and ESR)* One study [40] reported that Tongfengding capsules plus conventional treatment (allopurinol) significantly decreased CRP and ESR when compared to conventional treatment [Fig. 8; Analysis 1.5.1; MD −7.83 mg/L, 95% CI −9.26 to −6.40] and [Fig. 8; Analysis 1.5.2; MD −7.02 mg/L, 95% CI −8.48 to −5.56], respectively.

*Relapse rate* Two studies [41, 45] reported that Tongfengding capsules plus conventional treatment significantly decreased relapse rate when compared to conventional treatment [Fig. 9; Analysis 1.6; RR 0.24, 95% CI 0.09–0.61; $I^2$ = 0%].

*Adverse effects (rash, diarrhea, and gastrointestinal discomfort)* One study [41] reported that Tongfengding capsules plus conventional treatment significantly

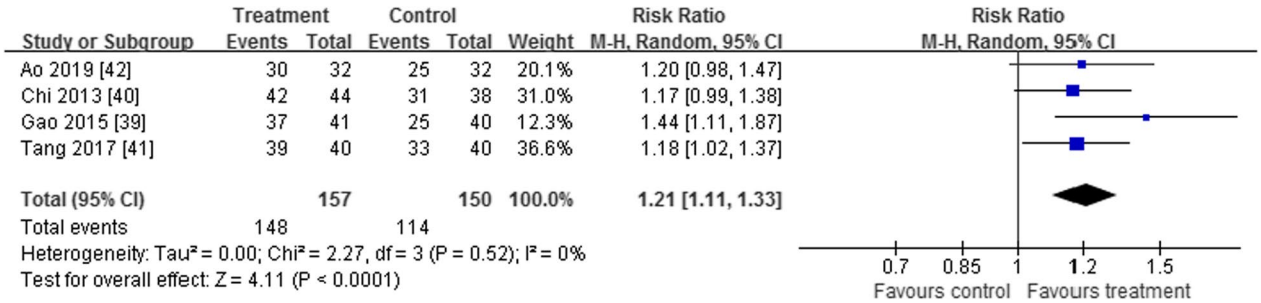


**Fig. 4** (Analysis 1.1): Comparison. Chinese patent medicine Tong-Feng-Ding-Jiao-Nang capsules plus conventional treatment versus conventional treatment. Outcome 1: Total effective rate

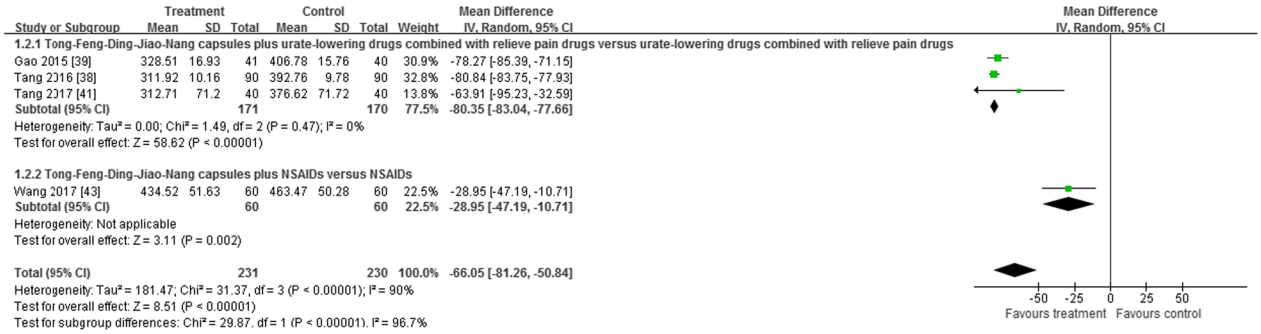


**Fig. 5** (Analysis 1.2): Chinese patent medicine Tongfengding capsules plus conventional treatment versus conventional treatment. Outcome 2: BUA. BUA: blood uric acid

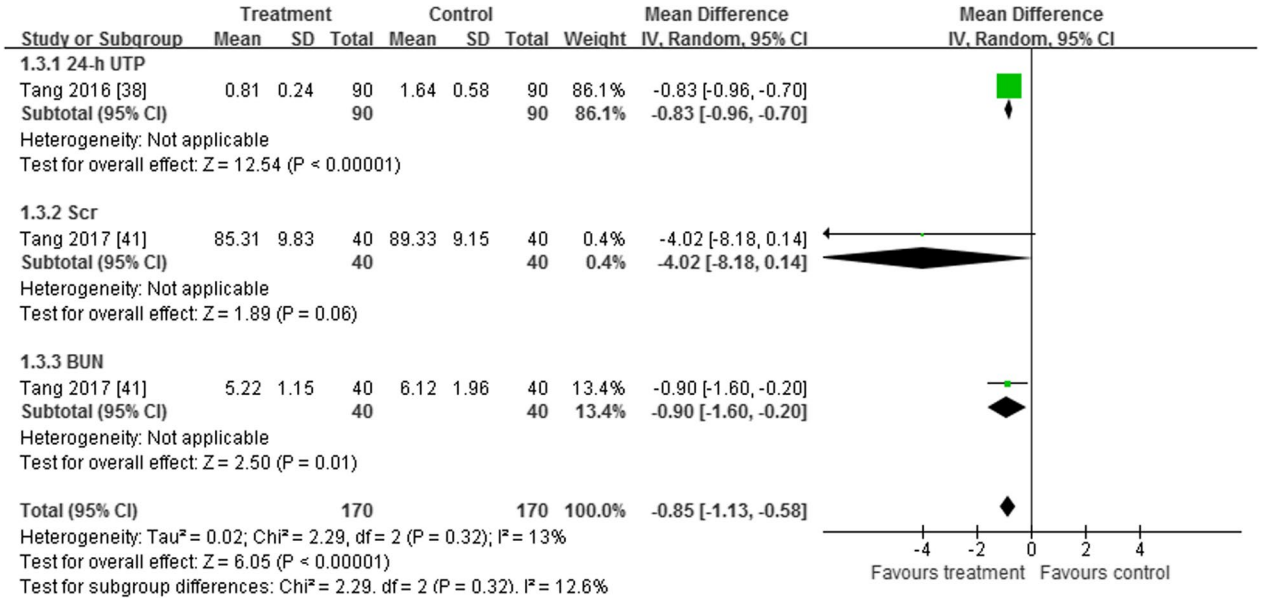


**Fig. 6** (Analysis 1.3): Chinese patent medicine Tongfengding capsules plus conventional treatment versus conventional treatment. Outcome 3: Kidney function (24-h UTP, SCr, and BUN). 24-h UTP: 24-h urinary total protein; SCr: serum creatinine; BUN: blood urea nitrogen

decreased adverse effects on overall effect when compared to conventional treatment [Fig. 10; Analysis 1.7; RR 0.21, 95% CI 0.04–0.95; $I^2 = 0\%$].

*Other outcomes* One study [42] reported no withdrawal symptoms, but provided no further details. All-cause mortality, economic index, and TCM tongue and pulse assessment (e.g., tongue coating and pulse) were not reported in any of the six studies.

### GRADE quality of evidence

The "GRADE profiler" provided by the Cochrane Collaboration Network was utilized to classify the results of this systematic review. The GRADE quality of evidence was moderate to high (Table 3).

## Discussion

Based on six RCTs [40–45] conducted in China, we found limited evidence that Chinese patent medicine Tongfengding capsule plus conventional treatment confers positive effects by increasing total effective rate and reducing BUA, 24-h UTP, BUN, IL-6, IL-8, TNF-α, CRP, ESR, relapse rate, and adverse effects (e.g., rash, diarrhea, and gastrointestinal discomfort), when compared with conventional treatment. However, there was insufficient evidence to confirm whether Chinese patent medicine Tongfengding capsules plus conventional treatment has positive effects on SCr, when compared with conventional treatment.

The quality of evidence in our review was high to moderate (Table 3: GRADE Quality of Evidence). The results

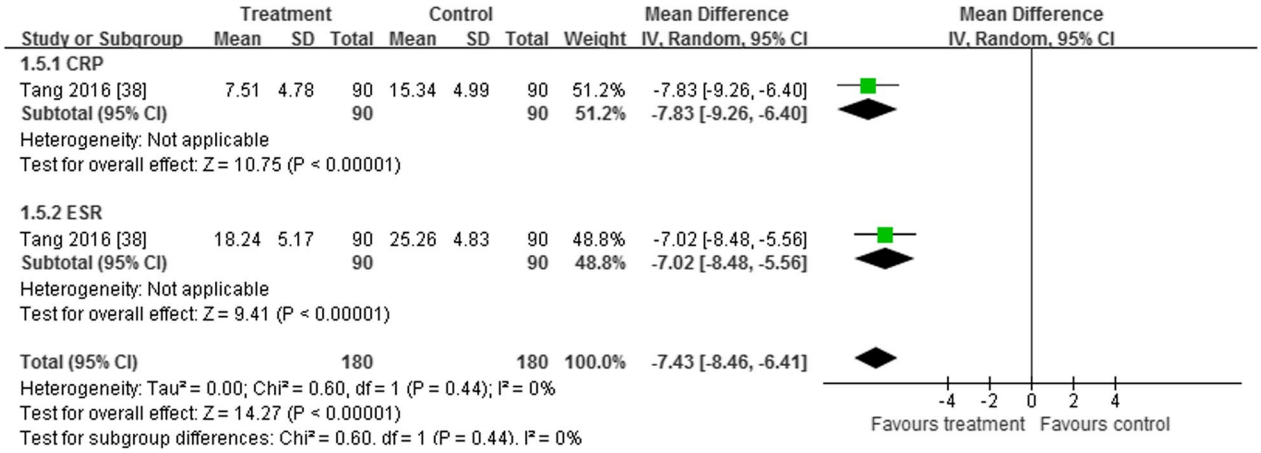


**Fig. 7** (Analysis 1.4): Chinese patent medicine Tongfengding capsules plus conventional treatment versus conventional treatment. Outcome 4: Inflammatory factor (IL-6, IL-8, and TNF-α). IL: interleukin, TNF-α: tumor necrosis factor-alpha

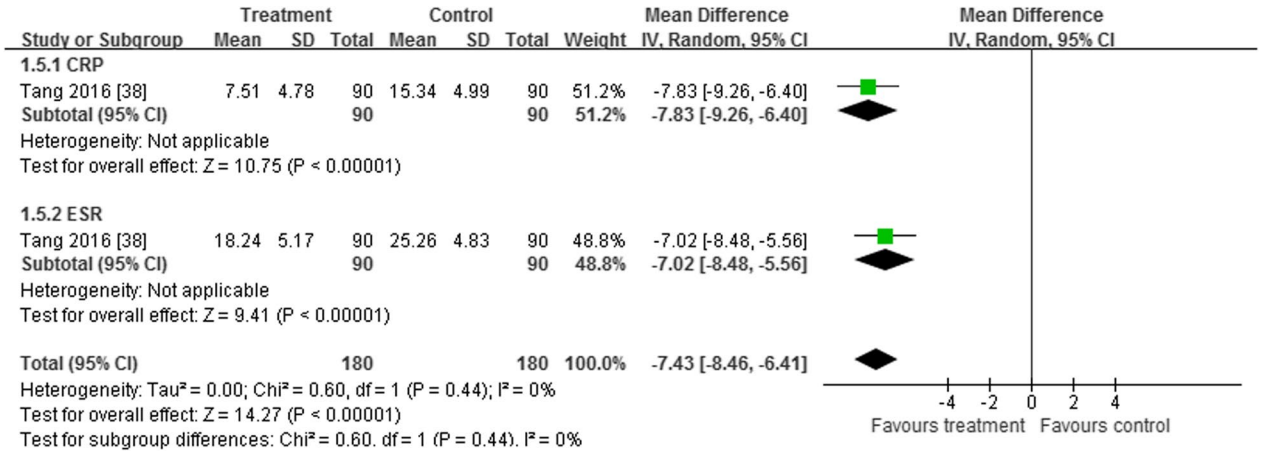


**Fig. 8** (Analysis 1.5): Chinese patent medicine Tongfengding capsules plus conventional treatment versus conventional treatment. Outcome 5: Related indicators (CRP and ESR). CRP: C-reactive protein; ESR: erythrocyte sedimentation rate

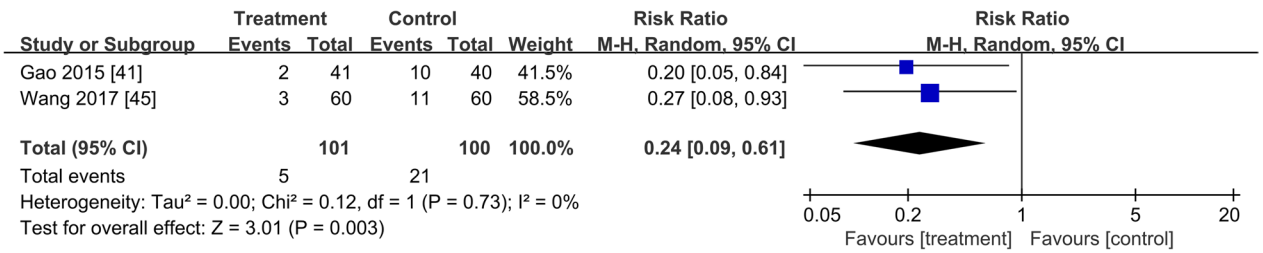


**Fig. 9** (Analysis 1.6): Chinese patent medicine Tongfengding capsules plus conventional treatment versus conventional treatment. Outcome 6. Relapse rate

were robust (e.g., further research is very unlikely to change and/or is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), but many studies were inadequately powered, and the methodological processes were either not described and/or flawed in many instances. For example, randomization was mentioned in two studies, but the randomization method was not reported [43,

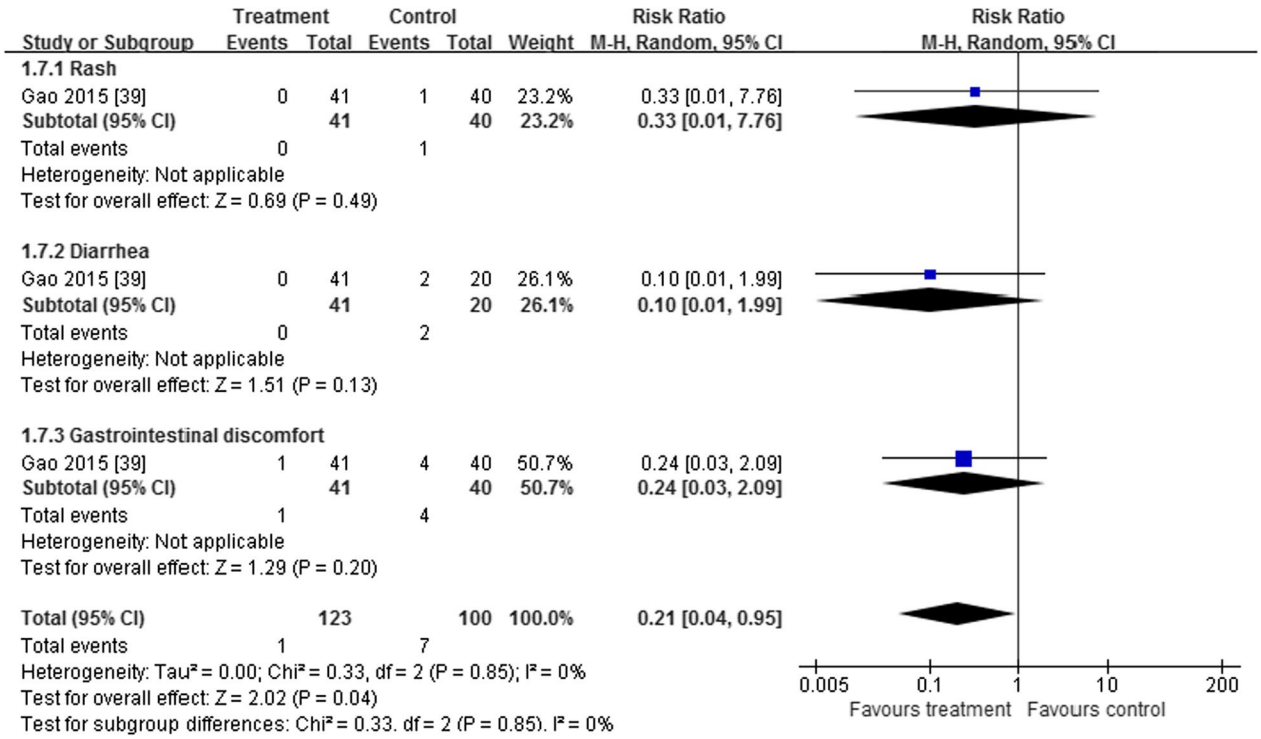


**Fig. 10** (Analysis 1.7): Chinese patent medicine Tongfengding capsules plus conventional treatment versus conventional treatment. Outcome 7: Adverse effects

44]; in the six included studies, allocation concealment was not mentioned [40–45], although telephone interviews with the original authors showed that allocation concealment was indeed used; in the six included trials, the blinding procedures were not mentioned [40–45], although the authenticity of blinding in three included trials was confirmed by telephone [43–45]. Consequently, the risks of performance and detection biases were unclear in the remaining three included studies [40–42]. In the review, despite our efforts to expand and clarify the reported data by contacting the original trial authors, we did not obtain significant and/or sufficient additional data to increase our assessments in one of the studies.

We determined that three of six included studies were of high methodological quality, three were of moderate methodological quality. Therefore, it is possible that these deficits may be wholly or partly related to the absence of sufficient reporting. We presume that selection, performance, and detection biases may have been present in the reviewed studies.

This evidence-based review investigated six RCTs of gout treatment among adults in China [40–45]. The six RCTs reported that Chinese patent medicine Tongfengding capsules (which acts by clearing heat, eliminating dampness, and activating blood to relieve pain) plus conventional treatment for gout demonstrated benefits through increased total effective rate and reduction of BUA, 24-h UTP, BUN, IL-6, IL-8, TNF-α, CRP, ESR, relapse rate, and adverse effects (e.g., rash, diarrhea, and gastrointestinal discomfort). Based on the findings of this review, the authors consider Chinese patent medicine Tongfengding capsules to be safe and beneficial in the management of gout when used in combination with conventional treatment. However, the results reported were from three studies with moderate methodological quality and three studies with high methodological quality.

Therefore, larger multicenter trials with high methodological quality are needed to assess further the use of Chinese patent medicine Tongfengding capsule in adults. These trials should include patients who have gout and are undergoing treatment with Tongfengding capsules. More data are necessary, particularly concerning TCM outcomes (such as tongue coating and pulse). The effect of Tongfengding capsule should also be explored based on TCM syndrome differentiation. Future trials should assess the most suitable treatment method, the role of Tongfengding capsule, and the optimal dosages for treatment of gout. Such studies would help to confirm the validity of our findings and could more clearly establish the efficacy of Tongfengding capsules for gout in adults, in comparison with other treatments.

**Table 3** GRADE quality of evidence

| **Tongfengding capsules plus conventional treatment versus conventional treatment for gout in adults** | | | | | | |
|---|---|---|---|---|---|---|
| **Patient or population: patients with gout in adults**<br>**Settings: inpatients or outpatients**<br>**Intervention: Tongfengding capsules plus conventional treatment versus conventional treatment** | | | | | | |
| **Outcomes** | **Illustrative comparative risks* (95% CI)** | | **Relative effect (95% CI)** | **No of Participants (studies)** | **Quality of the evidence (Grade)** | **Comments** |
| | **Assumed risk** | **Corresponding risk** | | | | |
| | **Control** | **Tongfengding capsules plus conventional treatment versus conventional treatment** | | | | |
| Total effective rate | Study population | | RR 1.21 (1.11–1.33) | 307 (4 studies) | ⊕⊕⊕⊕ high | Important |
| | 760 per 1000 | 920 per 1000 (844–1000) | | | | |
| | Moderate | | | | | |
| | 799 per 1000 | 967 per 1000 (887–1000) | | | | |
| BUA | | The mean bua in the intervention groups was 66.05 lower (81.26 to 50.84 lower) | | 461 (4 studies) | ⊕⊕⊕⊕ high | Important |
| Kidney function | | The mean kidney function in the intervention groups was 0.85 lower (1.13–0.58 lower) | | 340 (2 studies) | ⊕⊕⊕⊖ moderate[a] | Important |
| Inflammatory factors | | The mean inflammatory factors in the intervention groups was 9.18 lower (12.7–5.67 lower) | | 780 (2 studies) | ⊕⊕⊕⊖ moderate[a] | Important |
| Related indicators | | The mean related indicators in the intervention groups was 7.43 lower (8.46–6.41 lower) | | 360 (1 study) | ⊕⊕⊕⊖ moderate[b] | Important |
| Relapse rate | Study population | | RR 0.24 (0.09–0.61) | 201 (2 studies) | ⊕⊕⊕⊖ moderate[a] | Important |
| | 210 per 1000 | 50 per 1000 (19–128) | | | | |
| | Moderate | | | | | |
| | 217 per 1000 | 52 per 1000 (20–132) | | | | |
| Adverse effects | Study population | | RR 0.21 (0.04–0.95) | 223 (1 study) | ⊕⊕⊕⊖ moderate[b] | Important |
| | 70 per 1000 | 15 per 1000 (3–66) | | | | |
| | Moderate | | | | | |
| | 100 per 1000 | 21 per 1000 (4–95) | | | | |
| | Moderate | | | | | |
| | 25 per 1000 | 8 per 1000 (0–194) | | | | |
| | 100 per 1000 | 10 per 1000 (1–199) | | | | |
| | Moderate | | | | | |
| | 100 per 1000 | 10 per 1000 (1–199) | | | | |
| | 100 per 1000 | 24 per 1000 (3–209) | | | | |
| | Moderate | | | | | |
| | 100 per 1000 | 24 per 1000 (3–209) | | | | |

**Table 3** (continued)

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect. Handbook description: randomized controlled trial

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Cochrane Handbook description: relegation randomized controlled trial

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Cochrane Handbook description: two or more degradation factors of randomized controlled trials

Very low quality: We are very uncertain about the estimate. Cochrane Handbook description: more than three degradation factors of randomized controlled trials

Reduce the evidence quality factors: methodology defect, included in the research results of the inconsistency, indirect evidence, inexactness, and publication bias

Increase the level of evidence factor: large effect quantity, confounding factors cannot change effect quantity, or the existing concentration–response relationship

CI: Confidence interval; RR: Risk ratio

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI)

[a] Only two studies included

[b] Only one study included

### Limitations of study

One of the limitation of this study is its sample size. Due to small sample size, subgroup analysis results based on different type of drugs obtained was limited. Future studies may involve a larger size sample with high methodological quality. Besides, all the available data is in the Chinese population. Therefore, its application to other populations is limited at the moment.

## Conclusion

The Chinese patent medicine Tongfengding capsules plus conventional treatment is safe and beneficial for adults with gout when compared with conventional treatment.

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#### Author contributions

Guarantor of integrity of the entire study: QY. Study concepts: QY. Study design: QY. Definition of intellectual content: QY, XL. Literature research: QY, QH, YL, YL. Clinical studies: QY, QH, XL. Experimental studies: QY, QH, XL, YL. Data acquisition: QY, YL, YL. Data analysis: QY, KZ, AX. Statistical analysis: QY, QH, XL. Manuscript preparation: QY. Manuscript editing: QY, QH, XL, YL, YL, KZ, AX. Manuscript review: QY, XL.

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#### Availability of data and materials

The data used to support the findings of this study are available from the corresponding author upon request.

## Declarations

#### Ethics approval and consent to participate

All analyses were based on previous published studies,thus no ethical approval and patient consent are required.

#### Consent for publication

Informed consent was obtained.

#### Competing interests

The authors declare no competing interests.

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#### References

1. Pérez-Ruiz F, Jansen T, Tausche AK, et al. Efficacy and safety of lesinurad for the treatment of hyperuricemia in gout. Drug in Context. 2019;8:212581. https://doi.org/10.7573/dic.212581.
2. Lee HE, Yang G, Park YB, et al. Epigallocatechin-3-gallate prevents acute gout by suppressing NLRP3 inflammasome activation and mitochondrial DNA synthesis. Molecules. 2019;24(11):2138. https://doi.org/10.3390/molecules24112138.
3. Liu X, Liu K, Sun Q, et al. Efficacy and safety of febuxostat for treating hyperuricemia in patients with chronic kidney disease and in renal transplant recipients: a systematic review and meta-analysis. Exp Ther Med. 2018;16(3):1859–65.
4. Zhou L, Liu L, Liu XY, et al. Systematic review and meta-analysis of the clinical efficacy and adverse effects of Chinese herbal decoction for the treatment of gout. PLOS ONE. 2014;9(1):e85008.
5. Sinan Deveci O, Kabakci G, Okutucu S, et al. The association between serum uric acid level and coronary artery disease. Int J Clin Pract. 2010;64:900–7.
6. Ye RG. Internal medicine Chinese people's medical publishing house. 2001. p. 877–84.
7. Dang Q, Wang J, Zhang Y, et al. Study on the relationship between hyperuricemia andcardiovascular events in hypertension. J Pract Diagn Therapy. 2006;20:505–6.
8. Tsai CW, Lin SY, Kuo CC, et al. Serum uric acid and progression of kidney disease: a longitudinal analysis and mini-review. PLOS ONE. 2017;12:e0170393.
9. Arromdee E, Michet CJ, Crowson CS, et al. Epidemiology of gout: is the incidence rising? J Rheumatol. 2002;29:2403–6.
10. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007–2008. Arthritis Rheum. 2011;63:3136–41.
11. Collins MW, Saag KG, Singh JA. Is there a role for cherries in the management of gout? Therapeutic Adv Chronic Dis. 2019;11:1759720X19847018.
12. Chen-Xu M, Yokose C, Rai SK, et al. Contemporary prevalence of gout and hyperuricemia in the United States and decadal trends: the National Health and nutrition examination survey, 2007–2016. Arthritis Rheumatol. 2019. https://doi.org/10.1002/art.40807.

13. Kuo CF, Grainge MJ, Mallen C, et al. Rising burden of gout in the UK but continuing suboptimal management: a nationwide population study. Ann Rheum Dis. 2015;74(4):661–7.
14. Ting K, Hill C, Gill T, et al. Prevalence and associations of gout and hyperuricaemia: results from an Australian population-based study. Intern Med J. 2015;45:5.
15. Edward R, Doherty M. Epidemiology of gout. Arthritis Res Ther. 2010;12:223.
16. Li XX, Han M, Wang YY, et al. Chinese herbal medicine for gout: a systematic review of randomized clinical trials. Clin Rheumatol. 2013;32(7):943–59.
17. Wertheimer A, Morlock R, Becker MA. A revised estimate of the burden of illness of gout. Curr Ther Res Clin Exp. 2013;75:1–4.
18. Jones G, Panova E, Day R. Guideline development for the management of gout: role of combination therapy with a focus on lesinurad. Drug Des Dev Ther. 2017;11:3077–81.
19. Perez-Ruiz F, Martínez-Indart L, Carmona L, et al. Tophaceous gout and high level of hyperuricaemia are both associated with increased risk of mortality in patients with gout. Ann Rheum Dis. 2014;73(1):177–82.
20. Perez-Ruiz F, Castillo E, Chinchilla SP, et al. Clinical manifestations and diagnosis of gout. Rheum Dis Clin N Am. 2014;40(2):193–206.
21. Zhang W, Doherty M, Bardin T, et al. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR standing committee for international clinical studies including therapeutics (ESCISIT). Ann Rheum Dis. 2006;65:1312–24.
22. Graf SW, Whittle SL, Wechalekar MD, et al. Australian and New Zealand recommendations for the diagnosis and management of gout: integrating systematic literature review and expert opinion in the 3e Initiative. Int J Rheum Dis. 2015;18:341–51.
23. Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2017;76:29–42.
24. Qaseem A, Harris RP, Forciea MA. Management of acute and recurrent gout: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2017;166:58–68.
25. Hawkey CJ. Nonsteroidal anti-inflammatory drug gastropathy. Gastroenterology. 2000;119:521–35.
26. Graham DJ, Campen D, Hui R, et al. Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs: nested case-control study. Lancet. 2005;65:475–81.
27. Neogi T. Clinical practice. Gout. N Engl J Med. 2011;364:443–52.
28. Terkeltaub RA. Clinical practice. Gout. N Engl J Med. 2003;349:1647–55.
29. Richette P, Bardin T. Gout. Lancet. 2010;375:318–28.
30. Mikuls TR, MacLean CH, Olivieri J, et al. Quality of care indicators for gout management. Arthritis Rheum. 2004;50:937–43.
31. Baker JF, Schumacher HR. Update on gout and hyperuricemia. Int J Clin Pract. 2010;64:371–7.
32. Riedel AA, Nelson M, Wallace K, et al. Prevalence of comorbid conditions and prescription medication use among patients with gout and hyperuricemia in a managed care setting. JCR-J Clin Rheumatol. 2004;10:308–14.
33. Li T, Liu X, Zhang M, et al. Assessment of systematic reviews and meta-analyses on traditional chinese medicine published in Chinese journals. Chin J Evid Based Med. 2007;7:180–8.
34. Huedo-Medina TB, Sánchez-Meca J, Marín-Martínez F, et al. Assessing heterogeneity in meta-analysis: Q statistic or I2 index? Psychol Methods. 2006;11:193–206.
35. Multidisciplinary Expert Task Force on Hyperuricemia and Related Diseases. Chinese multidisciplinary expert consensus on the diagnosis and treatment of hyperuricemia and related diseases. Chin Med J 2017; 130:2473–88.
36. Higgins JP, Green S (editors). Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011]. The Cochrane Collaboration 2011. Available from https://www.cochrane-handbook.org
37. GRADEpro GDT: GRADEpro Guideline development tool [software]. McMaster University and Evidence Prime, 2022. Available from https://www.gradepro.org/.
38. Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available from https://www.guidelinedevelopment.org/handbook.
39. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analysis. BMJ. 2003;327(7174):227–60.
40. Tang L. Effect of allopurinol combined with Tongfengding capsule on inflammatory factors, hepatorenal functions, and related indicators in gouty patients. J Hainan Med Univ. 2016;22(21):2551–4.
41. Gao Y, Zhang ZR, Tang ZH, Lu J, Su Y. Clinical observation of Benzbromarone combined with Tongfengding capsules in treatment of gouty arthritis. Clin J Med Off. 2015;43(10):1060–2.
42. Chi S, Li K. Tongfengding capsule treat acute gouty arthritis randomized controlled study. J Pract Tradition Chin Internal Med. 2013;27(11):39–40.
43. Tang Y. Effect of febuxostat combined with Tongfengding capsule on inflammatory factors in patients with hyperuricemia. Mod J Integr Tradition Chin West Med. 2017;26(7):737–9.
44. Ao J. Observation on the curative effect of Tongfengding capsule in the treatment of senile gouty arthritis in the elderly. J Clin Med Lit. 2019;6(5):38–9.
45. Wang LJ, Xiang Y, Yang QF, Sun QJ. Effects of Tongfengding capsule combined with diclofenac sodium on blood uric acid level and joint swelling and pain score in gout patients. Chin J Biochem Pharm. 2017;37(8):83–4.


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