Herbal Medicine for Cervicogenic Dizziness: A Systematic Review and Meta-Analysis

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Research

Keywords: cervicogenic dizziness, herbal medicine, systematic review, meta-analysis

DOI: https://doi.org/10.21203/rs.3.rs-364098/v1

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Abstract

Background: Herbal medicines (HMs) have been widely used in the treatment of cervicogenic dizziness (CGD) based on their empirical effectiveness and safety. Herein, we reviewed and evaluated the clinical evidence on the efficacy and safety of HM for CGD.

Methods: Among the relevant studies published up to December 2019 in 11 electronic databases, only randomised controlled trials (RCTs) were included. The studies' methodological quality was assessed using the revised Cochrane risk-of-bias tool for randomised trials, and the strength of evidence for the main findings was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation approach.

Results: All 17 included RCTs with 1,797 participants were conducted with six types of modified HM prescriptions and three types of active controls. More than half of the included studies were of low quality because of the high risk of bias due to deviations from the intended intervention. HMs plus active controls were more effective in CGD treatment than active controls alone. HMs plus antivertigo drugs, HMs plus manual therapy, and HMs plus acupuncture therapy were all effective in CGD treatment, with HMs plus antivertigo drugs showing the most reliable effect. All HM prescriptions were effective for specific patterns of CGD when administered with active controls, with Banxia Baizhu Tianma tang and Dingxuan tang demonstrating the most reliable effect. No serious adverse events were reported in all included studies.

Conclusions: The current evidence suggests that HMs may enhance the treatment effect on CGD when combined with other treatments without serious adverse events. Further high-quality evidence is needed to draw a definite conclusion.

Systematic review registration: PROSPERO (registration number: CRD42020199222), and the Research Registry (Review Registry Unique Identifying Number: reviewregistry1036)

Background

Cervicogenic dizziness (CGD), a major categories of dizziness, is related to a variety of symptoms, such as headache, unsteadiness, lightheadedness, perception of spinning, nausea, and general disorientation, coexisting with neck pain or stiffness (1–4). Its prevalence is estimated to be 6.4–8.5% (5–7); however, CGD is common in older patients, particularly in those with cervical spine dysfunction. Therefore, there is growing apprehension that the number of patients with CGD will increase in accordance with the worldwide population ageing (8–10).

Although it is known that CGD originates from the cervical spine, its pathogenesis remains unclear (11). Until now, the most prevalent hypothesis is that CGD is caused by disharmony of proprioception of the cervical mechanoreceptors located in the joints, ligaments, and muscle spindles, which occurs when the proprioceptive system of the neck is damaged due to muscular fatigue, degeneration, or trauma (10, 12–14). In a recent review, CGD was classified based on the neuropathological mechanisms into neural types, comprising degenerative cervical spine disorder, whiplash-associated disorder, and Barré–Liéou syndrome, and vascular types, comprising Bow Hunter’s syndrome and Beauty Parlour syndrome. However, these diseases also overlap because they do not have completely distinct mechanisms (15). Because there are no established diagnostic criteria for CGD, physicians usually diagnose it when the patients’ symptoms are not related to other neurological or neuro-otological causes of dizziness (16, 17).

The treatment of CGD has not been standardised yet. Previous studies have explored a variety of treatments to improve the severity and frequency of dizziness by relaxing muscles and ameliorating abnormal proprioceptive sensitivity or impaired blood flow in the cervical region. Treatment strategies have included physical therapies (1, 3, 7, 10, 18–22), surgery (10, 16), topical drug injection (9, 23), acupuncture therapy (24, 25), and medications, such as muscle relaxants, opioids, nonsteroidal anti-inflammatory drugs, and anxiolytics, in combination with herbal medicines (HMs). HMs have been widely used for CGD, either alone or in combination with other treatments, based on their empirical effectiveness to suppress pain and improve blood circulation in the human body (24, 26). However, there has been no systematic verification of their efficacy and safety in the treatment of CGD based on clinical evidence.

Therefore, we aimed to review and evaluate the clinical evidence on the efficacy and safety of HMs as a monotherapy or adjunctive therapy for CGD, which would promote evidence-based decision-making in clinical practice.

Methods

Study registration

The study protocol for this systematic review was registered with the International Prospective Register of Systematic Reviews, PROSPERO (registration number: CRD42020199222) on October 27, 2020, and the Research Registry (Review Registry Unique Identifying Number: reviewregistry1036) on November 19, 2020. The study protocol was also published (27), and there have been no subsequent amendments that could cause a significant distortion in the study design. This review is reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement (28).

Data sources and search strategy

One researcher (H.O.) comprehensively searched the following 11 electronic databases for relevant studies published up to December 2019 without language or publication status restrictions: three English databases (Medical Literature Analysis and Retrieval System Online [MEDLINE] via PubMed, Excerpta Medica database [EMBASE] via Elsevier, and the Cochrane Central Register of Controlled Trials [CENTRAL]), six Korean databases (KoreanMed, Korean Studies Information Service System, Research Information Sharing Service, National Digital Science Library, Korean Medical Database, and Database Periodical Information Academic), one Chinese database (China National Knowledge Infrastructure), and one Japanese database (Citation Information by NII). A manual search on Google Scholar was also performed to identify additional eligible studies among those mentioned in the reference lists of included studies. The
search strategies were tailored to the language and search form of the databases. The search strategies used in three English databases (MEDLINE, EMBASE, and CENTRAL), set up broadly for sensitive searches, are presented in Additional file 1.

Eligibility criteria

1) Types of studies

All randomised controlled trials (RCTs) related to the use of HMs for CGD were included. Studies with any other design, including quasi-RCTs, were excluded.

2) Participants

All patients with CGD were considered as subjects of our study, with no restrictions on ethnicity, nationality, sex, age, or biological status.

3) Interventions and comparisons

HMs with any formulation administered orally, such as decoction, capsules, tablets, pills, and powders, were considered as experimental interventions. There was no limitation on the combination or number of herbs, HM dosage, or the frequency or duration of treatment. If the composition of the HMs used in the included studies was different from the original prescription, ‘Modified’ was indicated in front of the HM name. No treatment and placebo were considered as control interventions to identify the efficacy of HMs as monotherapy. Active controls, such as antivertigo drugs, manual therapy and acupuncture therapy, were also considered as control interventions to verify the efficacy of HMs as adjunctive therapy only when HMs were equally applied in both the experimental and control groups. Studies comparing different combinations of HMs or HMs alone with other active controls were excluded because they could not verify the efficacy of HMs rigorously.

4) Outcomes

The primary outcomes were as follows:

1. The change in the patients’ overall functional score measured by validated scales (e.g., Functional scale for cervical spondylosis of the vertebral artery type);
2. The change in the patients’ simple score for dizziness (e.g., numerical rating scale); and
3. The change in the average blood flow velocity in the vertebrobasilar artery, as evaluated using transcranial doppler.

The secondary outcomes were as follows:

1. The total effective rate, strictly calculated by counting only the number of patients completely cured, in order to exclude the subjectivity of researchers and improve the reliability of research results;
2. The change in haematological parameters, such as the levels of fibrinogen (Fib), endothelin (ET), total cholesterol (TC), and calcitonin gene-related peptide (CGRP); and
3. Adverse events.

Study selection

Two reviewers (H.O. and S.S.) independently screened and assessed all retrieved studies for eligibility based on the aforementioned criteria. After duplicates were removed, the titles and abstracts of the remaining studies were screened using EndNote X9. Next, full-text review of the eligible studies was conducted for final inclusion. Any divergence in agreement was resolved through discussion with the third researcher (E.L.) at each step of the study selection process.

Data extraction

Two reviewers independently extracted data from the included studies (H.O. and S.S.) using a predefined data acquisition form. This form included four main domains: general information (title, authors, year of publication, country of the study, and study design), participants’ characteristics (age, sex, diagnostic criteria, and CGD duration), intervention and comparison details (sample size, HM formulation and prescription name, number of herbs, HM dosage, HM daily dose, comparison, frequency or duration of the treatment, and follow-up information), and outcomes (primary and secondary outcomes and adverse events). Any discrepancy was resolved through discussion with the third researcher (E.L.).

Quality assessment

The methodological quality of the included studies was assessed using the revised Cochrane risk-of-bias tool for randomised trials (29). Bias domain for risk-of-bias assessment included the following: (1) bias arising from the randomisation process, (2) bias due to deviations from intended interventions, (3) bias due to missing outcome data, (4) bias in the outcome measurement, and (5) bias in the selection of the reported result. The risk of bias was independently evaluated by two reviewers (H.O. and S.S.) as ‘low’, ‘high’, or ‘some concerns’, and any divergence in agreement was resolved through discussion with other reviewers (E.L. and W.S.C.). Studies evaluated as ‘low-risk’ in all domains were defined as high-quality studies, whereas those evaluated as ‘high-risk’ in at least one domain were defined as low-quality studies.

Subsequently, the strength of the evidence for the main findings was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation approach (30). The risk of bias, inconsistency, indirectness and imprecision of the results, and publication bias were assessed, and the quality of the body of evidence was graded on a four-point scale as ‘high’, ‘moderate’, ‘low’, or ‘very low’.

Data synthesis

When the included studies were sufficiently homogenous, quantitative synthesis was performed using RevMan software version 5.3 (Cochrane, London, UK) to analyse the efficacy of HMs for the treatment of CGD. Subgroup analyses were conducted according to the (1) comparison types, and (2) HM prescription
names. Dichotomous outcomes were pooled using a risk ratio (RR), and continuous outcomes were pooled using a mean difference (MD) or standardised mean difference (SMD) with 95% confidence intervals (CIs).

Statistical heterogeneity among studies was assessed by computing $I^2$ statistics. Data were pooled using a random-effects model if the included studies had significant heterogeneity ($I^2$ values $\geq 50\%$ indicated substantial heterogeneity and those $\geq 75\%$ indicated considerable heterogeneity; both were considered as significant). Otherwise, a fixed-effects model was applied (31). Sensitivity analysis was performed to increase the robustness of the results by excluding studies with high risks of bias and outliers. If the number of studies was sufficient ($n \geq 10$), visual inspection of the funnel plot was performed to assess for publication bias. Data on the safety of HMs for CGD were described qualitatively.

## Results

### Study selection

A total of 7,735 studies were identified through the database searches, and one additional study was identified through other sources. After removing 305 duplicates, 6,765 studies were excluded by screening the titles and abstracts. Through review of the full-texts, 649 studies were further excluded: 17 studies with unavailable full-texts, 31 non-clinical studies, 21 case reports, 164 comparative studies, 5 nonrandomized controlled trials, 258 studies not related to CGD, 48 studies not related to eligible intervention, and 105 studies not related to the clinical question. Finally, 17 RCTs with 1,797 participants were included in the analysis (Fig. 1).

### Study characteristics

All included studies were RCTs conducted in China. They were classified according to the comparison types as follows: 1) studies comparing HMs plus antivertigo drugs with antivertigo drugs ($n = 6$), subdivided into studies prescribing flunarizine ($n = 3$) and those prescribing betahistine ($n = 3$); 2) studies comparing HMs plus manual therapy with manual therapy alone ($n = 5$); and 3) studies comparing HMs plus acupuncture therapy with acupuncture therapy alone ($n = 6$). There was no study which assessed the efficacy of HM as a monotherapy for CGD.

The included studies were also classified according to the HM prescription names as follows: 1) studies on Banxia Baizhu Tianma tang (BBTT) ($n = 5$); 2) study on Buzhong Yiqi tang (BYT) ($n = 1$); 3) studies on Dingxuan tang (DXT) ($n = 4$); 4) study on Guizhi Gegen tang (GGT) ($n = 1$); 5) study on Gegen Jieji tang (GJT) ($n = 1$); and 6) studies on Yiqi Congming tang (YCT) ($n = 5$). All HMs in the included studies were modified prescriptions. In summary, studies included in this review were conducted with six types of modified HM prescriptions (BBTT, BYT, DXT, GGT, GJT, and YCT), and three types of active controls (antivertigo drugs, manual therapy, and acupuncture therapy).

In addition, 10 types of outcome measurements were identified: two studies evaluated overall function scores, 11 studies evaluated simple scores, seven studies assessed the average blood flow velocity in the vertebral arteries, eight studies assessed the average blood flow velocity in the basilar artery, 16 studies evaluated the total effective rate, two studies measured the ET and CGRP levels, and three studies measured the Fib and TC levels. The incidence of adverse events was reported in only one study. The study characteristics and the main results are summarised in Table 1.
| Study ID | Sample size (A) : (B) | Sample of country | Mean age (yr) | CGD duration (range) | Intervention group (A) | Control group (B) | Treatment duration | Follow-up | Outcome | Results | AE (n) |
|----------|----------------------|-------------------|--------------|---------------------|-----------------------|-------------------|-------------------|-----------|---------|---------|--------|
| Dai 2018 (37) | 82 (41 : 41) | China | 46.2 ± 5.1 (3 ~ 11 mon) | NR | Modified YCT + (B) | AT (1time/day) | 4 weeks | NR | (1) TER | (A) > (B) * | NR |
| | | | | | | | | | | (2) Fib level | (A) > (B) * |
| | | | | | | | | | (3) TC level | (A) < (B) * |
| | | | | | | | | | (4) TER | (A) < (B) * |
| | | | | | | | | | (5) Fib level | (A) < (B) * |
| | | | | | | | | | (6) TC level | (A) < (B) * |
| | | | | | | | | | (7) SS | (A) > (B) † |
| | | | | | | | | | (8) OFS | (A) > (B) † |
| | | | | | | | | | (9) RVA-BF | (A) > (B) † |
| | | | | | | | | | (10) LVA-BF | (A) > (B) † |
| | | | | | | | | | (11) BA-BF | (A) > (B) † |
| | | | | | | | | | (12) TER | (A) > (B) † |
| | | | | | | | | | (13) Fib level | (A) > (B) † |
| | | | | | | | | | (14) TC level | (A) > (B) † |
| | | | | | | | | | (15) SS | (A) > (B) † |
| | | | | | | | | | (16) OFS | (A) > (B) † |
| | | | | | | | | | (17) RVA-BF | (A) > (B) † |
| | | | | | | | | | (18) LVA-BF | (A) > (B) † |
| | | | | | | | | | (19) BA-BF | (A) > (B) † |
| | | | | | | | | | (20) TER | (A) > (B) † |
| | | | | | | | | | (21) Fib level | (A) > (B) † |
| | | | | | | | | | (22) TC level | (A) > (B) † |
| | | | | | | | | | (23) SS | (A) > (B) † |
| | | | | | | | | | (24) OFS | (A) > (B) † |
| | | | | | | | | | (25) RVA-BF | (A) > (B) † |
| | | | | | | | | | (26) LVA-BF | (A) > (B) † |
| | | | | | | | | | (27) BA-BF | (A) > (B) † |
| | | | | | | | | | (28) TER | (A) > (B) † |
| | | | | | | | | | (29) Fib level | (A) > (B) † |
| | | | | | | | | | (30) TC level | (A) > (B) † |

Significant differences between the two groups are indicated as follows: * p < 0.05 and † p < 0.01. Insignificant differences between the two groups (p > 0.05) are indicated by N.S.

Abbreviations: AD, antivertigo drug; AE, adverse events; AT, acupuncture therapy; BA-BF, basilar artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong YiQi tang; CGD, cervicogenic dizziness; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fab, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; LVA-BF, left vertebral artery blood flow; MT, manual therapy; NR, not reported; OFS, Overall function score; RVA-BF, right vertebral artery blood flow; SS, simple score; TC, total cholesterol; TER, total effective rate; YCT, Yiqi Congming tang.
| Study ID | Sample size (A) : (B) | Study Of country | Mean age (range) | CGD duration (range) | Intervention group (A) | Control group (B) | Treatment duration | Follow-up | Outcome | Results | AE (n) |
|---------|----------------------|-------------------|-----------------|---------------------|-----------------------|---------------------|-------------------|----------|--------|--------|-------|
| Ji 2016 (34) | 60 (30 : 30) | China | NR (40 ~ 70) | NR | Modified DXT + (B) | AD: flunarizine (5mg qd) | 2 weeks | NR | (1) SS | (1) (A) > (B) * | (2) (A) > (B) * | NR |
| Liu 2019 (45) | 126 (63 : 63) | China | (A) 52.64 ± 8.25 (26 ~ 68) | (B) 52.47 ± 8.14 (22 ~ 65) | (A) 3.98 ± 1.02 yr (0.6 ~ 5 year) | Modified DXT + (B) | MT: Tuina (1time/day) | 4 weeks | NR | (1) SS | (1) (A) > (B) * | (2) (A) < (B) † | NR |
| Lyu 2017 (36) | 54 (27 : 27) | China | (A) 35.24 ± 2.15 (20 ~ 59) | (B) 31.17 ± 1.53 (18 ~ 60) | NR | Modified BYT + (B) | AT (1time/day) | 20 days | NR | (1) SS | (1) (A) > (B) * | (2) N.S. | NR |

Significant differences between the two groups are indicated as follows: * p < 0.05 and † p < 0.01. Insignificant differences between the two groups (p > 0.05) are indicated by N.S.

Abbreviations: AD, antivertigo drug; AE, adverse events; AT, acupuncture therapy; BA-BF, basilar artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CGD, cervicogenic dizziness; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; LVA-BF, left vertebral artery blood flow; MT, manual therapy; NR, not reported; OFS, Overall function score; RVA-BF, right vertebral artery blood flow; SS, simple score; TC, total cholesterol; TER, total effective rate; YCT, Yiqi Congming tang.
| Study ID | Sample size (A) : (B) | Study of country | Mean age (range) (yr) | CGD duration (range) | Intervention group (A) | Control group (B) | Treatment duration | Follow-up | Outcome | Results | AE (n) |
|----------|------------------------|-------------------|----------------------|----------------------|-----------------------|------------------|-------------------|-----------|---------|---------|--------|
| Pan 2019 | 100 (50: 50)           | China             | (A) 42.41 ± 5.93     | (A) 3.91 ± 0.74 mon  | Modified BBTT + (B)  | MT: Tuina (1 time/day) | 2 weeks          | NR        | (1) SS  | (1) (A) > (B) †  | Gastrointestinal discomfort (1) |
| Qin 2012 | 163 (79: 84)           | China             | 54.78 ± 10.36        | NR                   | Modified YCT + (B)   | AD: beta-histmine (18mg tid) | 2 weeks          | 3 months  | (1) SS  | (1) (A) > (B) †  |        |
| Qiu 2018 | 110 (55: 55)           | China             | (A) 53.8 ± 5.5       | (A) 4.5 ± 0.7 mon  | Modified YCT + (B)   | AT (1 time/day)       | 1 month          | NR        | (1) SS  | (1) (A) > (B) †  |        |
| Shang 2016 | 82 (41: 41)           | China             | 40.2 ± 1.7           | 3.1 ± 0.5 yr        | Modified GGT + (B)   | MT (qd)            | 2 weeks          | NR        | (1) SS  | (1) (A) > (B) †  |        |

Significant differences between the two groups are indicated as follows: † *p* < 0.01. Insignificant differences between the two groups (*p* > 0.05) are indicated by N.S.  

**Abbreviations:** AD, antivertigo drug; AE, adverse events; AT, acupuncture therapy; BA-BF, basilar artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yi Qi tang; CGD, cervicogenic dizziness; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; LVA-BF, left vertebral artery blood flow; MT, manual therapy; NR, not reported; OFS, Overall function score; RVA-BF, right vertebral artery blood flow; SS, simple score; TC, total cholesterol; TER, total effective rate; YCT, Yi Qi Congming tang.
| Study ID | Sample size (A) : (B) | Study of country | Mean age (range) (yr) | CGD duration (range) | Intervention group (A) | Control group (B) | Treatment duration | Follow-up | Outcome | Results | AE (n) |
|----------|----------------------|------------------|----------------------|----------------------|-----------------------|-------------------|-------------------|-----------|---------|---------|--------|
| Tan 2019 | 154 (77 : 77)        | China            | 23.6 ± 2.5 (18 ~ 30) | 37.6 ± 7.9 days (7 ~ 60 days) | Modified BBTT + (B) | AD: betahistine (16mg bid) | 10 days | NR | (1) TER | (1) (A) > (B) † | NR |
| Wang 2010 | 66 (34 : 32)        | China            | 35.34 ± 3.24 (20 ~ 64) | (A) 3.63 ± 1.45 yr (0.2 ~ 10 year) | Modified DXT + (B) | MT: Tuina (5times/week) | 4 weeks | NR | (1) SS | (2) TER | (1) (A) > (B) † | NR |
| Yang 2018 | 146 (73 : 73)       | China            | 35.72 ± 6.66 (18 ~ 54) | (A) 3.14 ± 0.75 mon (1 ~ 5 mon) | Modified YCT + (B) | AT (1time/day) | 2 weeks | NR | (1) RVA-BF | (2) RVA-BF | (3) BA-BF | (4) TER |
| Yao 2018  | 78 (39 : 39)        | China            | 42.17 ± 4.35 (22 ~ 58) | (A) 5.86 ± 1.35 yr (0.04 ~ 9 year) | Modified BBTT + (B) | AT (1time/day) | 6 weeks | NR | (1) RVA-BF | (2) RVA-BF | (3) BA-BF | (4) TER |
| Zhu 2019  | 120 (60 : 60)       | China            | (A) NR (31 ~ 59) | (A) NR (10 days ~ 3 year) | Modified DXT + (B) | MT: Tuina (1time/day) | 2 weeks | NR | (1) SS | (2) RVA-BF | (3) RVA-BF | (4) TER |

Significant differences between the two groups are indicated as follows: * p < 0.05 and † p < 0.01. Insignificant differences between the two groups (p > 0.05) are indicated by N.S.

Abbreviations: AD, antivertigo drug; AE, adverse events; AT, acupuncture therapy; BA-BF, basilar artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CGD, cervicogenic dizziness; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; LVA-BF, left vertebral artery blood flow; MT, manual therapy; NR, not reported; OFS, Overall function score; RVA-BF, right vertebral artery blood flow; SS, simple score; TC, total cholesterol; TER, total effective rate; YCT, Yiqi Congming tang.
Each HM prescription was applied to a specific pattern of symptoms in traditional Chinese medicine: BBTT to wind-phlegm type or phlegm stasis type; BYT to qi and blood deficiency type; DXT to spleen deficiency and dampness type, qi deficiency and blood stasis type, or hyperactivity of liver yang type; GGT to wind type with disharmony between ying and wei; GJT to collateral stasis type; and YCT to qi and blood deficiency type or qi deficiency and sputum silting up type. All modified HMs included at least one-third of the original prescriptions. The administration duration varied from 10 days to 8 weeks, with 2 weeks being the most frequent. The details of the HMs in the included studies are summarised in Table 2.
Table 2
Details of the herbal medicines in the included studies

| Study ID | Gao 2018 | Gu 2019 | Pan 2019 | Tan 2019 | Yao 2018 | Lyu 2017 | Ji 2016 | Liu 2019 | Wang 2010 | Zhu 2019 | Shang 2016 | Hu 2019 | Dai 2018 |
|----------|----------|----------|----------|----------|----------|----------|----------|----------|-----------|----------|------------|---------|----------|
| HM       | BBTT     | BYT      | DXT      | GGT      | GJT      | YCT      |
| Administration duration and frequency | 2wks, NR | 2wks, bid | 10dys, bid | 20dys, bid | 2wks, bid | 4wks, bid | 4wks, bid | 2wks, bid | 2wks, bid | 2wks, bid | 2wks, bid |
| HM dosage of components per day (g) | 12* | 7.5 | 10 | 9 | 10 | 10 | 20 | 20 | 12 |
| Atractylodis Rhizoma Alba | 12 | 6 | 10 | 6 | 9 | 9 | 5 | 9 | 10 |
| Glycyrrhizae Radix et Rhizoma | 9 | 10 | 6 | 9 | 5 | 9 | 10 | 6 |
| Citrus reticulata blanco | 6 | 9 | 6 | 9 | 5 | 9 | 10 | 6 |
| Gastrodiae Rhizoma | 12 | 9 | 9 | 10 | 10 | 12 | 10~15 | 15 | 12 |
| Pinelliae Tuber | 10 | 5 | 9 | 9 | 6 | 9 | 10 | 12 | 12 |
| Poria Sclerotium | 30 | 7.5 | 10 | 9 | 20 | 15 | 30 | 30 | 30 |
| Zingiberis Rhizoma Recens | 5 | 10 | 6 | 10 | 9 | 10 | 6 |
| Zizyphi Fructus | 2EA | 3EA | 10 | 10 | 15 | 10 | 12 | 30 |
| Angelicae Gigantis Radix | 12 | 10 | 10 | 15 | 10 | 20 | 30 | 30 | 30 |
| Bupleuri Radix | 6 | 9 | 10 | 12 | 10~15 | 15 | 10~30 | 12 | 12 |
| Codonopsis Pilosulae Radix | 6 | 9 | 10 | 12 | 10~15 | 15 | 10~30 | 12 | 12 |
| Ginseng Radix | 60 | 15 | 10 | 12 | 30 | 10 | 12 | 30 | 10 |
| Astragali Radix | 10 | 10 | 15 | 10 | 12 | 30 | 10 | 12 | 30 |
| Uncariae Ramulus cum Uncus | 10 | 10 | 15 | 10 | 12 | 30 | 10 | 12 | 30 |
| Salviae Miltiorrhizae Radix | 6 | 9 | 10 | 15 | 10~30 | 12 | 10~30 | 12 | 12 |
| Polygoni Multiflori Radix | 3 | 12 | NR | 10 | 12 | 30 | 10 | 12 | 30 |
| Scorpio | 7.5 | 10 | 10 | 15 | 30 | 9 | NR | 15 | NR |
| Paeoniae Radix | 10 | 9 | NR | 10 | 12 | 30 | 10 | 12 | 30 |
| Cinnamomi Ramulus | 5 | 10 | 9 | NR | 10 | 12 | 30 | 10 | 12 |
| Puerariae Radix | 30 | 20 | 30~60 | 15 | NR | 12 | 30 | 20 | 30~60 | 15 | NR | 12 |

Abbreviations: BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; DXT, Dingxuan tang; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; HM, herbal medicine

* The components included in the original prescription of each HM are marked in blue.
| Study ID | Gao 2018 | Gu 2019 | Pan 2019 | Tan 2019 | Yao 2018 | Lyu 2017 | Ji 2016 | Liu 2019 | Wang 2010 | Zhu 2019 | Shang 2016 | Hu 2019 | Dai 2018 |
|----------|----------|---------|----------|----------|----------|----------|---------|----------|----------|----------|-----------|---------|---------|
|          | (38)     | (43)    | (46)     | (47)     | (42)     | (36)     | (34)    | (45)     | (32)     | (48)     | (35)      | (44)    | (37)    |
| Ostericu seu Notopterygii Radix et Rhizoma | 10 | NR |
| Angelicae Dahuricae Radix | 10 | NR |
| Phellodendri Cortex | 12 |
| Viticis Fructus | 12 | 15 |
| Cnidii Rhizoma | 12 | 10 | 10 | 15 | 9 | 15~30 | 10 | NR |
| Alismatis Rhizoma | 10 | 30 | 20 | 20 |
| Arisaematis Rhizoma | 10 |
| Magnoliae Cortex | 12 |
| Phyllostachyos Caulis in Taeniam | 7.5 |
| Aurantii Fructus Immaturus | 6 |
| Myrrha | 10 |
| Olibanum | 10 |
| Fossilia Ossis Mastodi | 30 | 30 |
| Ostreae Testa | 30 | 30 | 30 |
| Nelumbinis Folium | 15 |
| Zingiberis Rhizoma | 9 |
| Margaritiferae Usta Concha | 30 |
| Loranthi Ramulus Et Folium | 12 |
| Polygalae Radix | NR |
| Ligustici Tenuissimi Rhizoma et Radix | NR |
| Eleocharitis rhizoma |  |

**Abbreviations:** BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; DXT, Dingxuan tang; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; HM, herbal m Congming tang

* The components included in the original prescription of each HM are marked in blue.

**Risk-of-bias assessment**

For the bias arising from the randomisation process, seven studies were evaluated as ‘low-risk’ because the randomisation process for the allocation sequence was clearly described. The remaining 10 studies were determined as ‘some concerns’ because the relevant information was provided insufficiently. For the bias due to deviations from intended interventions, 11 studies, most of which were studies with manual or acupuncture therapy as active controls, were judged as ‘high-risk’ because it was unclear whether blinding of participants and trial personnel had been sufficiently performed by using sham-massage or sham-
acupuncture. The remaining six studies were determined as ‘some concerns’. For the bias due to missing outcome data, 13 studies were evaluated as ‘low-risk’ and one study was judged as ‘high-risk’ because there was missing data, but only the result of per protocol analysis was reported. The remaining three studies were determined as ‘some concerns’ because of insufficient provision of the relevant information. For the bias in the measurement of the outcome, eight studies were evaluated as ‘low-risk’ and the remaining nine studies were determined as ‘some concerns’ because it was difficult to judge whether outcome indicators used in the studies were affected by the awareness of outcome assessors. For the bias in the selection of the reported results, all studies were evaluated as ‘some concerns’ because there was no basis for judging, such as study protocols. Finally, for the overall risk of bias, 11 studies were evaluated as low-quality studies because they were assessed as ‘high-risk’, and the remaining six studies were evaluated ‘some concerns’ (Fig. 2).

**Efficacy: HMs plus active controls vs. active controls alone**

In the total analysis on all included studies, compared with active controls alone, HMs plus active controls significantly decreased the overall function scores (two studies; SMD 1.54, 95% CI 1.22 to 1.86, \( I^2 = 0 \% \)), and TC level (three studies; MD 0.58, 95% CI 0.24 to 0.91, \( I^2 = 80\% \)). In addition, HMs plus active controls significantly increased the simple scores (11 studies; SMD 1.14, 95% CI 0.44 to 1.84, \( I^2 = 96\% \)), the blood flow velocity in the left vertebral artery (seven studies; MD 4.81, 95% CI 3.37 to 6.25, \( I^2 = 86\% \)), right vertebral artery (seven studies; MD 3.80, 95% CI 2.12 to 5.47, \( I^2 = 90\% \)), and the basilar artery (eight studies; MD 6.49, 95% CI 3.23 to 9.75, \( I^2 = 97\% \)), and the CGRP level (two studies; MD 4.63, 95% CI 2.25 to 7.00, \( I^2 = 93\% \)), and improved the total effective rate (16 studies; RR 1.66, 95% CI 1.45 to 1.90, \( I^2 = 0\% \)). However, the change in the ET (two studies; MD 16.48, 95% CI -0.34 to 33.31, \( I^2 = 98\% \)) and Fib levels (three studies; MD 0.32, 95% CI -0.02 to 0.66, \( I^2 = 96\% \)) showed no significant difference between the intervention and control groups.

**Efficacy: HMs plus each active control vs. active control alone**

1. **HMs plus antivertigo drugs vs. antivertigo drugs alone**

In the subanalysis of the six studies using antivertigo drugs as active control, compared with antivertigo drugs alone, HMs plus antivertigo drugs significantly increased the simple scores (three studies; SMD 1.21, 95% CI 0.12 to 2.31, \( I^2 = 96\% \)) and the blood flow velocity in the left vertebral artery (one study; MD 5.01, 95% CI 4.27 to 5.75), right vertebral artery (one study; MD 4.65, 95% CI 3.75 to 5.55), and basilar artery (one study; MD 5.27, 95% CI 4.01 to 6.53). HMs plus antivertigo drugs also significantly improved the total effective rate (five studies; RR 1.63, 95% CI 1.27 to 2.08, \( I^2 = 0\% \)). Moreover, in the additional subanalysis by components of the antivertigo drugs, the combinations of HMs and flunarizine (three studies; RR 1.60, 95% CI 1.22 to 2.09, \( I^2 = 0\% \)) and HMs and betahistine (two studies; RR 1.69, 95% CI 1.01 to 2.82, \( I^2 = 0\% \)) both significantly improved the total effective rate.

2. **HM plus manual therapy vs. manual therapy alone**

In the subanalysis of the five studies using manual therapy as active control, compared with manual therapy alone, HMs plus manual therapy significantly decreased the overall function scores (one study; SMD 1.49, 95% CI 1.09 to 1.89), and increased the blood flow velocity in the left vertebral artery (two studies; MD 3.81, 95% CI 2.84 to 4.79, \( I^2 = 0\% \)) and right vertebral artery (two studies; MD 3.48, 95% CI 2.52 to 4.44, \( I^2 = 0\% \)), and the CGRP level (two studies; MD 4.63, 95% CI 2.25 to 7.00, \( I^2 = 93\% \)). Furthermore, HMs plus manual therapy significantly improved the total effective rate (five studies; RR 1.73, 95% CI 1.34 to 2.23, \( I^2 = 0\% \)). However, the change in the simple scores (five studies; SMD 0.63, 95% CI -0.60 to 1.87, \( I^2 = 97\% \)), blood flow velocity in the basilar artery (two studies; MD 2.96, 95% CI -0.27 to 6.19, \( I^2 = 74\% \)), and ET level (two studies; MD 16.48, 95% CI -0.34 to 33.31, \( I^2 = 98\% \)) showed no significant difference compared with the control group.

3. **HM plus acupuncture therapy vs. acupuncture therapy alone**

In the subanalysis of the six studies using acupuncture therapy as active control, compared with acupuncture therapy alone, HMs plus acupuncture therapy significantly decreased the overall function scores (one study; SMD 1.64, 95% CI 1.09 to 2.18) and TC level (three studies; MD 0.58, 95% CI 0.24 to 0.91, \( I^2 = 80\% \)). In addition, HMs plus acupuncture therapy significantly increased the simple scores (three studies; SMD 1.93, 95% CI 1.11 to 2.75, \( I^2 = 85\% \)) and the blood flow velocity in the left vertebral artery (four studies; MD 5.39, 95% CI 2.10 to 8.68, \( I^2 = 92\% \)), right vertebral artery (four studies; MD 3.83, 95% CI 0.35 to 7.30, \( I^2 = 94\% \)), and basilar artery (five studies; MD 8.15, 95% CI 1.87 to 14.43, \( I^2 = 98\% \)), and improved the total effective rate (six studies; RR 1.64, 95% CI 1.33 to 2.03, \( I^2 = 0\% \)). However, the change in the Fib level (three studies; MD 0.32, 95% CI -0.02 to 0.66, \( I^2 = 96\% \)) showed no statistically significant difference between the intervention and control groups.

**Efficacy: each HM plus active controls vs. active controls alone**

1. **BBTT plus active controls vs. active controls alone**

In the subanalysis of the five studies using BBTT, compared with active controls alone, BBTT plus active controls significantly decreased the ET level (one study; MD 25.13, 95% CI 21.29 to 28.97) and increased the simple scores (one study; SMD 0.62, 95% CI 0.22 to 1.02), the blood flow velocity in the left vertebral artery (two studies; MD 4.44, 95% CI 3.18 to 5.69, \( I^2 = 71\% \)), right vertebral artery (two studies; MD 3.85, 95% CI 2.29 to 5.41, \( I^2 = 84\% \)), and basilar artery (two studies; MD 3.48, 95% CI 0.04 to 6.92, \( I^2 = 95\% \)), and the CGRP level (one study; MD 5.89, 95% CI 4.78 to 7.00). BBTT plus active controls also significantly improved the total effective rate (five studies; RR 1.75, 95% CI 1.39 to 2.19, \( I^2 = 0\% \)).

2. **BYT plus active controls vs. active controls alone**

In the subanalysis of the one study using BYT, compared with acupuncture therapy alone, BYT plus acupuncture therapy significantly increased the simple scores (one study; SMD 1.10, 95% CI 0.53 to 1.68). However, the change in the blood flow velocity in the left vertebral artery (one study; MD 1.22, 95% CI -0.61
to 3.05), right vertebral artery (one study; MD -1.47, 95% CI -3.04 to 0.10), and basilar artery (one study; MD 0.31, 95% CI -1.48 to 2.10), and the total effective rate (one study [40]; RR 1.33, 95% CI 0.53 to 3.33) showed no significant difference between the intervention and control groups.

3. **DXT plus active controls vs. active controls alone**

In the subanalysis of the four studies using DXT, compared with active controls alone, DXT plus active controls significantly decreased the overall function scores (one study; SMD 1.49, 95% CI 1.09 to 1.89) and ET level (one study; MD 7.96, 95% CI 5.39 to 10.53), and increased the blood flow velocity in the left vertebral artery (two studies; MD 3.81, 95% CI 2.84 to 4.79, $I^2 = 0\%$) and right vertebral artery (two studies; MD 3.48, 95% CI 2.52 to 4.44, $I^2 = 0\%$), and the CGRP level (one study; MD 3.46, 95% CI 2.91 to 4.01). Moreover, DXT plus active controls significantly improved the total effective rate (four studies; RR 1.57, 95% CI 1.16 to 2.11, $I^2 = 0\%$). However, the change in the simple scores (four studies; SMD 0.54, 95% CI -1.08 to 2.16, $I^2 = 98\%$) and blood flow velocity in the basilar artery (two studies; MD 2.96, 95% CI -0.27 to 6.19, $I^2 = 74\%$) showed no statistically significant difference between the intervention and control groups.

4. **GGT plus active controls vs. active controls alone**

In the subanalysis of the one study using GGT, compared with manual therapy alone, GGT plus manual therapy significantly increased the simple scores (one study; SMD 1.44, 95% CI 0.95 to 1.93) and improved the total effective rate (one study; RR 1.83, 95% CI 1.05 to 3.19).

5. **GJT plus active controls vs. active controls alone**

In the subanalysis of the one study using GJT, GJT plus antivertigo drug (betahistine) significantly increased the change in the simple scores (one study; SMD 2.12, 95% CI 1.76 to 2.47), compared with the antivertigo drug alone. However, the total effective rate (one study; RR 2.19, 95% CI 0.99 to 4.86) showed no significant difference compared with the control group.

6. **YCT plus active controls vs. active controls alone**

In the subanalysis of the five studies using YCT, compared with active controls alone, YCT plus active controls significantly decreased the overall function scores (one study; SMD 1.64, 95% CI 1.09 to 2.18) and TC levels (three studies; MD 0.58, 95% CI 0.24 to 0.91, $I^2 = 80\%$), and increased the simple scores (three studies; SMD 1.70, 95% CI 0.28 to 3.12, $I^2 = 96\%$) and the blood flow velocity in the left vertebral artery (two studies; MD 8.59, 95% CI 3.59 to 13.58, $I^2 = 87\%$), right vertebral artery (two studies; MD 7.05, 95% CI 5.30 to 8.81, $I^2 = 0\%$), and basilar artery (three studies; MD 13.04, 95% CI 6.06 to 20.03, $I^2 = 95\%$).

Furthermore, YCT plus active controls significantly improved the total effective rate (four studies; RR 1.56, 95% CI 1.23 to 1.98, $I^2 = 0\%$). However, the change in the Fib levels (three studies; MD 0.32, 95% CI -0.02 to 0.66, $I^2 = 96\%$) demonstrated no statistically significant difference between the intervention and control groups.

Summarising the results of the subanalysis according to HM prescription names, BBTT, DXT, and YCT showed significant treatment effects in various primary and secondary outcomes, and had relatively more clinical evidence compared to the remaining HM prescriptions. Each of BYT, GGT, and GJT were investigated in only one clinical RCT. In the GGT study, one primary outcome (change in the simple scores) and one secondary outcome (total effective rate) were statistically significant. However, in the BYT and GJT studies, only one primary outcome (change in the simple scores) was significant, whereas the other outcomes were not statistically significant. The results of the total analysis and the subanalyses on the efficacy of HMs are shown in Table 3.
## Table 3
### Summary of findings

| Outcomes        | No. of Participants (RCTs) | Anticipated absolute effects (95% CI) | Relative Effect with HM group (95% CI) | I² value | Quality of evidence (GRADE) | Comments |
|-----------------|---------------------------|---------------------------------------|---------------------------------------|----------|-----------------------------|----------|
| **Risk with control group** |                          |                                        |                                       |          |                             |          |
| **No. of Participants** |                          |                                        |                                       |          |                             |          |
| **Outcomes**    |                           |                                        |                                       |          |                             |          |
| Total analysis  |                           |                                        |                                       |          |                             |          |
| OFS             | 196 (2)                   | SMD 1.54 higher (1.22–1.86 higher)    | –                                     | 0%       | ⊕⊕⊕⊕ Moderate              | Risk of bias (-1) |
| SS              | 1151 (11)                 | SMD 1.14 higher (0.44–1.84 higher)    | –                                     | 96%      | ⊕●●● Very low             | Risk of bias (-1) |
| LVA-BF          | 700 (7)                   | MD 4.81 higher (3.37–6.25 higher)     | –                                     | 86%      | ⊕●●● Low                  | Risk of bias (-1) |
| RVA-BF          | 700 (7)                   | MD 3.80 higher (2.12–5.47 higher)     | –                                     | 90%      | ⊕●●● Very low             | Risk of bias (-1) |
| BA-BF           | 810 (8)                   | MD 6.49 higher (3.23–9.75 higher)     | –                                     | 97%      | ⊕●●● Low                  | Risk of bias (-1) |
| TER             | 1,634 (16)                | 416 per 1,000 (373–489)               | RR 1.66 (1.45–1.90)                   | 0%       | ⊕⊕⊕⊕ Moderate              | Risk of bias (-1) |
| ET level (vs. MN) | 226 (2)                   | MD 16.48 higher (0.34 lower-33.31 higher) | – | 98% | ⊕●●● Very low | Risk of bias (-1) |

If the evidence of more than two studies showed MD < 4 for the change in the blood flow velocity in the vertebrobasilar artery or RR > 2 for the total effective rate, it was considered that there was a strong association for a treatment effect.

**Abbreviation:** AD, anti-vertigo drugs; AT, acupuncture therapy; BA-BF, basal artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CI, confidence interval; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; HM, herbal medicine; LVA-BF, left vertebral artery blood flow; MD, mean difference; MT, manual therapy; OFS, Overall function score; RCT, randomized controlled trial; RR, risk ratio; RVA-BF, right vertebral artery blood flow; SMD, standardized mean difference; SS, simple score; TER, total effective rate; YCT, Yiqi Congming tang
| Outcomes                  | No. of Participants (RCTs) | Anticipated absolute effects (95% CI) | Relative Effect (95% CI) | $\chi^2$ value | Quality of evidence (GRADE) | Comments |
|---------------------------|----------------------------|--------------------------------------|--------------------------|----------------|------------------------------|----------|
|                           |                            | Risk with control group              | Risk with HM group       |                |                              |          |
| CGRP level (vs. MN)       | 226 (2)                    | –                                    | MD 4.63 higher (2.25–7.00 higher) | –              | 93%                          | ⊕⊕⊕○     | Risk of bias (-1)
|                           |                            |                                      |                          |                |                              | Inconsistency (-2) |
| Fib level (vs. AT)        | 262 (3)                    | –                                    | MD 0.32 higher (0.02 lower–0.66 higher) | –              | 96%                          | ⊕⊕⊕○     | Risk of bias (-1)
|                           |                            |                                      |                          |                |                              | Inconsistency (-2) |
|                           |                            |                                      |                          |                |                              | Imprecision (-1) |
| TC level (vs. AT)         | 262 (3)                    | –                                    | MD 0.58 higher (0.24–0.91 higher) | –              | 80%                          | ⊕⊕○○     | Risk of bias (-1)
|                           |                            |                                      |                          |                |                              | Inconsistency (-2) |

2. Subgroup analysis according to the comparison types

2.1. HM plus AD vs. AD

|                           |                            |                                      |                          |                |                              |          |
| SS                       | 423 (3)                    | –                                    | SMD 1.21 higher (0.12–2.31 higher) | –              | 96%                          | ⊕⊕⊕○     | Risk of bias (-1)
|                           |                            |                                      |                          |                |                              | Inconsistency (-2) |
| LVA-BF (vs. flunarizine) | 106 (1)                    | –                                    | MD 5.01 higher (4.27–5.75 higher) | –              | N/A                          | ⊕⊕○○     | Risk of bias (-1)
|                           |                            |                                      |                          |                |                              | Moderate (-1) |
| RVA-BF (vs. flunarizine) | 106 (1)                    | –                                    | MD 4.65 higher (3.75–5.55 higher) | –              | N/A                          | ⊕⊕○○     | Risk of bias (-1)
|                           |                            |                                      |                          |                |                              | Moderate (-1) |
| BA-BF (vs. flunarizine)  | 106 (1)                    | –                                    | MD 5.27 higher (4.01–6.53 higher) | –              | N/A                          | ⊕⊕○○     | Risk of bias (-1)
|                           |                            |                                      |                          |                |                              | Moderate (-1) |
| TER                      | 600 (5)                    | 229 per 1,000                        | 347 per 1,000 (290–475) | RR 1.63 (1.27–2.08) | 0%                           | ⊕⊕○○     | Risk of bias (-1)
|                           |                            |                                      |                          |                |                              | Moderate (-1) |
| TER (vs. flunarizine)    | 246 (3)                    | 366 per 1,000                        | 585 per 1,000 (446–765) | RR 1.60 (1.22–2.09) | 0%                           | ⊕⊕○○     | Risk of bias (-1)
|                           |                            |                                      |                          |                |                              | Moderate (-1) |

If the evidence of more than two studies showed MD < 4 for the change in the blood flow velocity in the vertebrobasilar artery or RR > 2 for the total effective rate, it was considered that there was a strong association for a treatment effect.

Abbreviation: AD, anti-vertigo drugs; AT, acupuncture therapy; BA-BF, basal artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CI, confidence interval; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; HM, herbal medicine; LVA-BF, left vertebral artery blood flow; MD, mean difference; MT, manual therapy; OFS, Overall function score; RCT, randomized controlled trial; RR, risk ratio; RVA-BF, right vertebral artery blood flow; SMD, standardized mean difference; SS, simple score; TER, total effective rate; YCT, Yiqi Congming tang
| Outcomes | No. of Participants (RCTs) | Anticipated absolute effects (95% CI) | Relative Effect (95% CI) | \( \hat{\sigma} \) value | Quality of evidence (GRADE) | Comments |
|----------|---------------------------|--------------------------------------|--------------------------|-----------------|-----------------------------|----------|
| TER      | 354 (2)                   | 121 per 1,000                        | RR 1.69                  | 0%              | ⊕⊕⊕○                        | Risk of bias |
|         |                           | 198 per 1,000                        |                          |                 |                             |          |
| (vs. betahistine) |                   | (122–341)                         | (1.01–2.82)              |                 | (-1)                        |          |

### 2.2. HM plus MT versus MT

| Abbreviation | Study | Participants (RCTs) | Relative Effect (95% CI) | \( \hat{\sigma} \) value | Quality of evidence (GRADE) | Comments |
|--------------|-------|---------------------|--------------------------|-----------------|-----------------------------|----------|
| OFS          | 126 (1) | –                   | SMD 1.49 higher (1.09–1.89 higher) | N/A              | ⊕⊕⊕○                        | Risk of bias (-1) |
| SS           | 494 (5) | –                   | SMD 0.63 higher (0.60 lower-1.87 higher) | 97%             | ⊕⊕⊕                    | Risk of bias (-1) Inconsistency (2) Imprecision (-1) |
| LVA-BF       | 246 (2) | –                   | MD 3.81 higher (2.84–4.79 higher) | 0%              | ⊕⊕⊕○                        | Risk of bias (-1) |
| RVA-BF       | 246 (2) | –                   | MD 3.48 higher (2.52–4.44 higher) | 0%              | ⊕⊕⊕○                        | Risk of bias (-1) |
| BA-BF        | 246 (2) | –                   | MD 2.96 higher (0.27 lower-6.19 higher) | 74%             | ⊕⊕⊕                    | Risk of bias (-1) Inconsistency (1) Imprecision (1) |

Abbreviation: AD, anti-vertigo drugs; AT, acupuncture therapy; BA-BF, basal artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CI, confidence interval; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; HM, herbal medicine; LVA-BF, left vertebral artery blood flow; MD, mean difference; MT, manual therapy; OFS, Overall function score; RCT, randomized controlled trial; RR, risk ratio; RVA-BF, right vertebral artery blood flow; SMD, standardized mean difference; SS, simple score; TER, total effective rate; YCT, Yiqi Congming tang

If the evidence of more than two studies showed MD < 4 for the change in the blood flow velocity in the vertebrobasilar artery or RR > 2 for the total effective rate, it was considered that there was a strong association for a treatment effect.
| Outcomes | No. of Participants (RCTs) | Anticipated absolute effects (95% CI) | Relative Effect (95% CI) | I² value | Quality of evidence (GRADE) | Comments |
|----------|---------------------------|--------------------------------------|--------------------------|----------|-----------------------------|----------|
|          | Risk with control group   | Risk with HM group  |
| TER      | 494 (5)                   | 236 per 1,000                       | 411 per 1,000 (316–526) | RR 1.73 (1.34–2.23) | 0% ⊕⊕⊕⊕ Moderate | Risk of bias (-1) |
|          | 2.3. HM plus AT versus AT |
| OFS      | 70 (1)                    | –                                    | SMD 1.64 higher (1.09–2.18 higher) | – N/A | ⊕⊕⊕⊕ Moderate | Risk of bias (-1) |
| SS       | 234 (3)                   | –                                    | SMD 1.93 higher (1.11–2.75 higher) | – 85% | ⊕⊕⊕ Very low | Risk of bias (-1) Inconsistency (-2) |
| LVA-BF   | 348 (4)                   | –                                    | MD 5.39 higher (2.10–8.68 higher) | – 92% | ⊕⊕⊕⊕ Low | Risk of bias (-1) Inconsistency (-2) Strong association (+1) |
| RVA-BF   | 348 (4)                   | –                                    | MD 3.48 higher (3.01–3.97 higher) | – 94% | ⊕⊕⊕ Very low | Risk of bias (-1) Inconsistency (-2) |

If the evidence of more than two studies showed MD < 4 for the change in the blood flow velocity in the vertebrobasilar artery or RR > 2 for the total effective rate, it was considered that there was a strong association for a treatment effect.

Abbreviation: AD, anti-vertigo drugs; AT, acupuncture therapy; BA-BF, basal artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CI, confidence interval; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; HM, herbal medicine; LVA-BF, left vertebral artery blood flow; MD, mean difference; MT, manual therapy; OFS, Overall function score; RCT, randomized controlled trial; RR, risk ratio; RVA-BF, right vertebral artery blood flow; SMD, standardized mean difference; SS, simple score; TER, total effective rate; YCT, Yiqi Congming tang
| Outcomes | No. of Participants (RCTs) | Anticipated absolute effects (95% CI) | Relative Effect (95% CI) | \( \chi^2 \) value | Quality of evidence (GRADE) | Comments |
|----------|---------------------------|---------------------------------------|--------------------------|-----------------|---------------------------|----------|
|          |                           | Risk with HM group                    | Risk with control group  |                 |                           |          |
| BA-BF    | 458 (5)                   | MD 8.15 higher (1.87–14.43 higher)   | –                        | 98%             | @@@@                     | Low      |
|          |                           |                                       |                          |                 |                           | Risk of bias |
|          |                           |                                       |                          |                 |                           | (-1)     |
|          |                           |                                       |                          |                 |                           | Inconsistency |
| TER      | 540 (6)                   | 504 per 1,000 (409–624)               | RR 1.64 (1.33–2.03)     | 0%              | @@@@                     | Moderate |
|          |                           |                                       |                          |                 |                           | (-1)     |
|          |                           |                                       |                          |                 |                           |          |
| 3. Subgroup analysis according to the HM prescription names |
| 3.1. BBTT plus active controls vs. active controls |
| SS       | 100 (1)                   | SMD 0.62 higher (0.22–1.02 higher)   | –                        | N/A             | @@@@                     | Moderate |
|          |                           |                                       |                          |                 |                           | (-1)     |
| LVA-BF   | 184 (2)                   | MD 4.44 higher (3.18–5.69 higher)    | –                        | 71%             | @@@@                     | Moderate |
|          |                           |                                       |                          |                 |                           | (-1)     |
|          |                           |                                       |                          |                 |                           | Inconsistency |
|          |                           |                                       |                          |                 |                           | (-1)     |
|          |                           |                                       |                          |                 |                           | Strong association (+1) |
| RVA-BF   | 184 (2)                   | MD 3.85 higher (2.29–5.41 higher)    | –                        | 84%             | @@@@                     | Very low |
|          |                           |                                       |                          |                 |                           | (-1)     |
|          |                           |                                       |                          |                 |                           | Inconsistency |
|          |                           |                                       |                          |                 |                           | (2)      |

If the evidence of more than two studies showed MD < 4 for the change in the blood flow velocity in the vertebrobasilar artery or RR > 2 for the total effective rate, it was considered that there was a strong association for a treatment effect.

Abbreviation: AD, anti-vertigo drugs; AT, acupuncture therapy; BA-BF, basal artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CI, confidence interval; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; HM, herbal medicine; LVA-BF, left vertebral artery blood flow; MD, mean difference; MT, manual therapy; OFS, Overall function score; RCT, randomized controlled trial; RR, risk ratio; RVA-BF, right vertebral artery blood flow; SMD, standardized mean difference; SS, simple score; TER, total effective rate; YCT, Yiqi Congming tang
| Outcomes          | No. of Participants (RCTs) | Anticipated absolute effects (95% CI) | Relative Effect (95% CI) | $\hat{\text{i}}^2$ value | Quality of evidence (GRADE) | Comments                |
|-------------------|----------------------------|--------------------------------------|--------------------------|----------------------------|-----------------------------|--------------------------|
| BA-BF             | 184 (2)                    | MD 3.48 higher                       | -                        | 95%                        | ⊗●●●                       | Risk of bias             |
| (0.04–6.92 higher)|                            |                                      |                          |                            |                             |                          |
| TER               | 518 (5)                    | 274 per 1,000                        | 479 per 1,000           | RR 1.75                    | ⊗⊗⊗⊗                      | Risk of bias             |
| (381–600)         |                            | (1.39–2.19)                          |                          |                            |                             |                          |
| ET level          | 100 (1)                    | MD 25.13 higher                      | -                        | N/A                        | ⊗⊗⊗⊗                      | Risk of bias             |
|                   |                            | (21.29–28.97 higher)                 |                          |                            |                             |                          |

If the evidence of more than two studies showed MD < 4 for the change in the blood flow velocity in the vertebrobasilar artery or RR > 2 for the total effective rate, it was considered that there was a strong association for a treatment effect.

Abbreviation: AD, anti-vertigo drugs; AT, acupuncture therapy; BA-BF, basal artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CI, confidence interval; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; HM, herbal medicine; LVA-BF, left vertebral artery blood flow; MD, mean difference; MT, manual therapy; OFS, Overall function score; RCT, randomized controlled trial; RR, risk ratio; RVA-BF, right vertebral artery blood flow; SMD, standardized mean difference; SS, simple score; TER, total effective rate; YCT, Yiqi Congming tang
| Outcomes       | No. of Participants (RCTs) | Anticipated absolute effects (95% CI) | Relative Effect (95% CI) | $\chi^2$ value | Quality of evidence (GRADE) | Comments |
|----------------|---------------------------|--------------------------------------|--------------------------|----------------|-----------------------------|----------|
|                |                           | Risk with control group              | Risk with HM group       |                |                             |          |
| CGRP level     | 100 (1)                   | MD 5.89 higher (4.78-7.00 higher)    | N/A                      | @@@●          | Moderate                    | Risk of bias (-1) |
| 3.2. BYT plus active controls vs. active controls |                           |                                      |                          |                |                             |          |
| SS             | 54 (1)                    | SMD 1.10 higher (0.53–1.68 higher)   | N/A                      | @@@●          | Moderate                    | Risk of bias (-1) |
| LVA-BF         | 54 (1)                    | MD 1.22 higher (0.61 lower-3.05 higher) | N/A                      | @@@●          | Low                         | Risk of bias (-1) Imprecision (-1) |
| RVA-BF         | 54 (1)                    | MD 1.47 lower                      | N/A                      | ●●●●          | Very low                    | Risk of bias (-1) Imprecision (-1) |
| BA-BF          | 54 (1)                    | MD 0.31 higher (1.48 lower-2.10 higher) | N/A                      | @@@●          | Low                         | Risk of bias (-1) Imprecision (-1) |

If the evidence of more than two studies showed MD < 4 for the change in the blood flow velocity in the vertebrobasilar artery or RR > 2 for the total effective rate, it was considered that there was a strong association for a treatment effect.

Abbreviation: AD, anti-vertigo drugs; AT, acupuncture therapy; BA-BF, basal artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CI, confidence interval; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; HM, herbal medicine; LVA-BF, left vertebral artery blood flow; MD, mean difference; MT, manual therapy; OFS, Overall function score; RCT, randomized controlled trial; RR, risk ratio; RVA-BF, right vertebral artery blood flow; SMD, standardized mean difference; SS, simple score; TER, total effective rate; YCT, Yiqi Congming tang
| Outcomes          | No. of Participants (RCTs) | Anticipated absolute effects (95% CI) | Relative Effect (95% CI) | $i^2$ value | Quality of evidence (GRADE) | Comments                  |
|-------------------|-----------------------------|---------------------------------------|--------------------------|-------------|-----------------------------|---------------------------|
| TER               | 54 (1)                      | 222 per 1,000 (118–740)               | RR 1.33 (0.53–3.33)      | N/A         | N/A                         | Risk of bias (-1)          |
|                   |                             |                                       |                          |             |                             | Imprecision (-1)           |
|                   |                             |                                       |                          |             |                             |                           |
| 3.3. DXT plus active controls vs. active controls |                             |                                       |                          |             |                             |                           |
| OFS               | 126 (1)                     | SMD 1.49 higher (1.09–1.89 higher)    | –                        | N/A         | N/A                         | Risk of bias (-1)          |
|                   |                             |                                       |                          |             |                             |                           |
| SS                | 372 (4)                     | SMD 0.54 higher (1.08 lower-2.16 higher) | –                        | 98%         | N/A                         | Risk of bias (-1)          |
|                   |                             |                                       |                          |             |                             | Inconsistency (-2)          |
|                   |                             |                                       |                          |             |                             |                           |
| LVA-BF            | 246 (2)                     | MD 3.81 higher (2.84–4.79 higher)     | –                        | 0%          | N/A                         | Risk of bias (-1)          |
| RVA-BF            | 246 (2)                     | MD 3.48 higher (2.52–4.44 higher)     | –                        | 0%          | N/A                         | Risk of bias (-1)          |

If the evidence of more than two studies showed MD < 4 for the change in the blood flow velocity in the vertebrobasilar artery or RR > 2 for the total effective rate, it was considered that there was a strong association for a treatment effect.

Abbreviation: AD, anti-vertigo drugs; AT, acupuncture therapy; BA-BF, basal artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CI, confidence interval; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; HM, herbal medicine; LVA-BF, left vertebral artery blood flow; MD, mean difference; MT, manual therapy; OFS, Overall function score; RCT, randomized controlled trial; RR, risk ratio; RVA-BF, right vertebral artery blood flow; SMD, standardized mean difference; SS, simple score; TER, total effective rate; YCT, Yiqi Congming tang
| Outcomes | No. of Participants (RCTs) | Anticipated absolute effects (95% CI) | Risk with HM group | Relative Effect (95% CI) | I² value | Quality of evidence (GRADE) | Comments |
|----------|---------------------------|--------------------------------------|-------------------|-------------------------|---------|-----------------------------|----------|
| BA-BF    | 246 (2)                   | –                                    | MD 2.96 higher (0.27 lower–6.19 higher) | –                  | 74%     | ⊕⊕⊕○                         | Risk of bias (-1) Inconsistency (-1) Imprecision (-1) |
| TER      | 372 (4)                   | 232 per 1,000                        | 369 per 1,000 (270–490) | RR 1.57 (1.16–2.11) | 0%      | ⊕⊕⊕○                         | Risk of bias (-1) |
| ET level | 126 (1)                   | –                                    | MD 7.96 higher (5.39–10.53 higher) | –                  | N/A     | ⊕⊕⊕○                         | Risk of bias (-1) |
| CGRP level | 126 (1)              | –                                    | MD 3.46 higher (2.91–4.01 higher) | –                  | N/A     | ⊕⊕⊕○                         | Risk of bias (-1) |
| 3.4. GGT plus active controls vs. active controls | | | | | | | |
| SS       | 82 (1)                    | –                                    | SMD 1.44 higher (0.95–1.93 higher) | –                  | N/A     | ⊕⊕⊕○                         | Risk of bias (-1) |
| TER      | 82 (1)                    | 293 per 1,000                        | 537 per 1,000 (307–934) | RR 1.83 (1.05–3.19) | N/A     | ⊕⊕⊕○                         | Risk of bias (-1) |
| 3.5. GJT plus active controls vs. active controls | | | | | | | |
| SS       | 200 (1)                   | –                                    | SMD 2.12 higher (1.76–2.47 higher) | –                  | N/A     | ⊕⊕⊕○                         | Risk of bias (-1) |
| TER      | 200 (1)                   | 88 per 1,000                         | 187 per 1,000 (87–425) | RR 2.19 (0.99–4.86) | N/A     | ⊕⊕⊕○                         | Risk of bias (-1) Imprecision (-1) |
| 3.6. YCT plus active controls vs. active controls | | | | | | | |
| OFS      | 70 (1)                    | –                                    | SMD 1.64 higher (1.09–2.18 higher) | –                  | N/A     | ⊕⊕⊕○                         | Risk of bias (-1) |
| SS       | 1151 (3)                  | –                                    | SMD 1.70 higher (0.28–3.12 higher) | –                  | 96%     | ⊕⊕⊕○ Very low                | Risk of bias (-1) Inconsistency (2) |

If the evidence of more than two studies showed MD < 4 for the change in the blood flow velocity in the vertebrobasilar artery or RR > 2 for the total effective rate, it was considered that there was a strong association for a treatment effect.

Abbreviation: AD, anti-vertigo drugs; AT, acupuncture therapy; BA-BF, basal artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CI, confidence interval; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; HM, herbal medicine; LVA-BF, left vertebral artery blood flow; MD, mean difference; MT, manual therapy; OFS, Overall function score; RCT, randomized controlled trial; RR, risk ratio; RVA-BF, right vertebral artery blood flow; SMD, standardized mean difference; SS, simple score; TER, total effective rate; YCT, Yiqi Congming tang
| Outcomes | No. of Participants (RCTs) | Anticipated absolute effects (95% CI) | Relative Effect (95% CI) | | Quality of evidence (GRADE) | Comments |
|----------|---------------------------|--------------------------------------|--------------------------|-----------------|-----------------------------|-----------|
| LVA-BF   | 216 (2)                   | MD 8.59 higher (3.59–13.58 higher)   | –                        | 87%             | @@@@                        | Risk of bias (-1) Inconsistency (-2) Strong association (+1) |
| RVA-BF   | 216 (2)                   | MD 7.05 higher (5.30–8.81 higher)    | –                        | 0%              | @@@@@                       | Risk of bias (-1) Strong association (+1) |
| BA-BF    | 326 (3)                   | MD 13.04 higher (6.06–20.03 higher)  | –                        | 95%             | @@@@                        | Risk of bias (-1) Inconsistency (-2) Strong association (+1) |
| TER      | 408 (4)                   | 326 per 1,000 (398–641)              | RR 1.56 (1.23–1.98)      | 0%              | @@@@                        | Risk of bias (-1) |
| Fib level | 262 (3)                   | MD 0.32 higher (0.02 lower–0.66 higher) | –                        | 96%             | @@@@                        | Risk of bias (-1) Inconsistency (-2) Imprecision (-1) |
| TC level | 262 (3)                   | MD 0.58 higher (0.24–0.91 higher)    | –                        | 80%             | @@@@                        | Risk of bias (-1) Inconsistency (-2) |

If the evidence of more than two studies showed MD < 4 for the change in the blood flow velocity in the vertebrobasilar artery or RR > 2 for the total effective rate, it was considered that there was a strong association for a treatment effect.

Abbreviation: AD, anti-vertigo drugs; AT, acupuncture therapy; BA-BF, basal artery blood flow; BBTT, Banxia Baizhu Tianma tang; BYT, Buzhong Yiqi tang; CI, confidence interval; CGRP, calcitonin gene-related peptide; DXT, Dingxuan tang; ET, endothelin; Fib, fibrinogen; GGT, Guizhi Gegen tang; GJT, Gegen Jieji tang; GRADE, the Grading of Recommendations Assessment, Development, and Evaluation; HM, herbal medicine; LVA-BF, left vertebral artery blood flow; MD, mean difference; MT, manual therapy; OFS, Overall function score; RCT, randomized controlled trial; RR, risk ratio; RVA-BF, right vertebral artery blood flow; SMD, standardized mean difference; SS, simple score; TER, total effective rate; YCT, Yiqi Congming tang

Safety

Of the 17 studies, only one study reported an adverse event; one case of gastrointestinal discomfort, evaluated as not serious, was reported in the BBTT plus manual therapy group (Table 1).

Quality of evidence
In the comparison of HMs plus active controls with active controls alone, the quality of evidence for the primary outcomes ranged from 'very low' to 'moderate'. For the secondary outcomes, the quality of evidence for the total effective rate was graded as 'moderate', but that for the other outcomes was graded as 'very low'. In other words, the overall quality of evidence in the total analysis was rated 'low'.

In the comparison of HMs plus antivertigo drugs with antivertigo drugs alone, the quality of evidence for all outcomes, except for the simple scores, was graded as 'moderate'. In the comparison of HMs plus manual therapy with manual therapy alone, the quality of evidence for most outcomes was graded as 'moderate', but that for the simple scores and the blood flow velocity in the basilar artery was graded as 'very low'. In the comparison of HMs plus acupuncture therapy with acupuncture therapy alone, the quality of evidence for the overall functional scores and the total effective rate was graded as 'moderate', but that for the other outcomes ranged from 'very low' to 'low'. In summary, in the subanalysis according to the comparison types, the overall quality of evidence was higher, but decreasing in the order of HMs plus antivertigo drugs, HMs plus manual therapy, and HMs plus acupuncture therapy.

In the comparison of BBTT plus active controls with active controls alone, the quality of evidence for most outcomes, except for the blood flow velocity in the right vertebral and basilar arteries, was graded as 'moderate'. Similarly, in the comparison of DXT plus active controls with active controls alone, the quality of evidence for most outcomes, except for the simple scores and the blood flow velocity in the basilar artery, was graded as 'moderate'. In the comparison of GGT plus active controls with active controls alone, the quality of evidence for the simple scores and the total effective rate was also graded as 'moderate'. In the comparison of GJT plus active controls with active controls alone, the quality of evidence for the simple scores was graded as 'moderate', but that for the total effective rate was graded as 'low'. In the comparison of YCT plus active controls with active controls alone, the quality of evidence for outcomes ranged from 'very low' to 'high'. Finally, in the comparison of BYT plus active controls with active controls alone, the quality of evidence for outcomes ranged from 'very low' to 'moderate'. In summary, in the subanalysis according to HM prescription names, the overall quality of evidence was highest for BBTT, DXT, and GGT, and lowest for BYT. The main reason for the downgrade was the high risk of bias for the included studies, and the inconsistency of the results due to high heterogeneity between them (Table 3).

Publication bias
For two outcomes included in more than 10 studies, we checked for publication bias through funnel plot analysis. In the comparison of HMs plus active controls with active controls alone, the overall functional scores showed asymmetry, suggesting the existence of potential publication bias (Fig. 3); thus, there may be negative results not published in the literature. Conversely, the funnel plot for the total effective rate was symmetrical (Fig. 4).

Discussion
In this study, we reviewed and evaluated the available clinical evidence on the efficacy and safety of HMs as monotherapy or adjunctive therapy for the treatment of CGD to promote evidence-based decision-making in clinical practice. Since none of the included 17 RCTs (32–48) could assess the efficacy of HMs for CGD as monotherapy, we evaluated only their efficacy as adjunctive therapy used with other active controls. The included studies were conducted with six types of modified HM prescriptions and three types of active controls. In the risk-of-bias assessment, more than half of the included studies were evaluated to be of low quality because of the high risk of bias due to deviations from the intended intervention. The results of the efficacy analyses for HMs plus active controls indicated the following. First, HMs plus active controls were more effective in CGD treatment than active controls alone (administration duration varied from 10 days to 8 weeks). Second, HMs plus antivertigo drugs (flunarizine and betahistine), HMs plus manual therapy, and HMs plus acupuncture therapy were all effective in CGD treatment. Among all, HMs plus antivertigo drugs showed the most reliable effect. Third, BBTT, BYT, DXT, GGT, GJT, and YCT were effective for specific patterns in patients with CGD, when administered with active controls. Among the HM prescriptions, BBTT and DXT had the most reliable effect when combined with active controls. Regarding the safety of HMs plus active controls in the treatment of CGD, no serious adverse events were reported in all included studies.

In traditional Chinese medicine, HMs are prescribed to match the specific pattern of patients' signs and symptoms. It is reasonable to select and prescribe the most appropriate HM for a specific pattern in each patient with CGD, as opposed to consistently prescribing one HM prescription to all patients with CGD, even if it is statistically the most evidenced prescription for CGD. Thus, although BBTT and DXT had the highest level of clinical evidence for the treatment effect on CGD in this review, it may be more effective to use other HM prescriptions for certain patterns in some patients with CGD. BBTT, which has the effect of dispelling pathogenic wind and eliminating phlegm, is used for the wind-phlegm type. Several studies have reported quantitative clinical evidence for the use of BBTT with antivertigo drugs (38, 43, 47). DXT has the effect of removing a pathogenic mass as the original prescription, and it can be prescribed for both deficiency and excess syndromes by modification of the original prescription. HMs can be modified for better efficacy and fewer side effects (49). In cases of combined excess and deficiency syndromes, such as spleen deficiency and dampness type, or qi deficiency and blood stasis type, DXT was modified by addition of herbs that have effects on invigorating the qi and spleen (Codonopsis Pilosulae Radix, and Atractylodis Rhizoma Alba), regulating qi-flowing (Citri Reticulatae Pericarpium), enriching the blood (Angelicae Gigantis Radix), and soothing the nerves (Floschasiae Ossis Mastodi), but with subtraction of other herbs from the original prescription, which have effects on suppressing hyperactive liver for calming endogenous wind (Uncariae Ramulus cum Uncus, and Scorpio) and promoting blood circulation with removing blood stasis (Salviae Miltiorrhizae Radix) (34, 45). On the other hand, in cases of only excess syndrome, such as hyperactivity of liver yang type, DXT was modified by adding Puerariae Radix, which has the effect of dispelling wind-heat (32, 48). For the combination of DXT and other treatments, quantitative clinical evidence has been reported for the use of DXT with manual therapy (32, 45, 48). Both YCT (33, 37, 39–41) and BYT (36) are used for the qi and blood deficiency type. However, YCT has a higher quality clinical evidence than BYT, because BYT showed low precision for outcomes. For the combination of YCT and other treatments, the most quantitatively reported clinical evidence was for the use of YCT with acupuncture therapy (37, 39–41). Additionally, GGT was used with manual therapy for the wind type with disharmony between ying and weil (35), and GJT was used for the collateral stasis type with betahistine (44). Through this review, we obtained a clue about the corresponding relation of patterns in patients with CGD and HM prescriptions; however, it remains unknown which HM prescription is the most effective for a certain pattern in these patients, because all included studies used only one HM prescription with one pattern of patients with CGD. Further studies are needed to confirm which HM prescription is the most effective in a certain pattern in these patients.
In this review, we identified Fib, ET, TC, and CGRP as haematological indicators used in clinical studies on CGD. ET and CGRP were used as indicators to verify the efficacy of HMs plus manual therapy compared with manual therapy alone. Fib and TC were used to verify the efficacy of HMs plus acupuncture therapy compared with acupuncture therapy alone. ET is an endogenous vasoconstrictor that reduces the perfusion of brain tissues by constricting the blood vessels in the brain (50, 51). CGRP is a vasodilator mainly distributed in the central nervous system (52). In a previous study, ET and CGRP were reported as important factors affecting the development of CGD with vertebrobasilar arteriospasm (53). Furthermore, Fib is able to promote the formation of atherosclerotic plaques (54), and TC is able to accelerate atherosclerosis and cause lipid metabolism disorders (55). In summary, control of the ET and CGRP levels improves the prognosis of CGD, and evaluation of the Fib and TC levels help predict CGD progression (38). Therefore, it can be recommended to use them as outcomes when conducting further clinical trials for CGD.

This review has some limitations. First, the quality of the included RCTs was generally poor, in particular, because of the high risk of bias due to deviations from the intended intervention. Second, most meta-analyses showed high heterogeneity among studies. Third, potential publication bias could not be ruled out, because the assessment of publication bias was not conducted in the meta-analyses in which the number of included studies was less than 10, and all RCTs were conducted in China and published in Chinese. Fourth, there is a possibility of attrition bias, because few studies presented dropout or withdrawal statistics. Fifth, it was unknown whether the treatment effect of HMs plus active controls maintained after completion of the intervention, because most studies did not perform follow-up assessments. Finally, the safety of HMs for CGD is still unclear, because few studies had clearly reported that there were no adverse events.

However, this research is valuable as the first systematic review that comprehensively evaluated the efficacy and safety of HMs for treating CGD and will aid clinicians to select and prescribe HMs suitable for specific patterns of patients with CGD based on evidence-based decision-making. Furthermore, it provides knowledge of which treatments will be effective in combination with HMs. Thereby, this research may contribute for the development of effective strategies in the treatment and management of the increasing number of patients with CGD due to population ageing. Nonetheless, further high-quality evidence from rigorously conducted clinical studies, preferably conducted outside of China, is required to support the clinical recommendations regarding the use of HMs for CGD. In addition, placebo-controlled RCTs are needed to evaluate the efficacy of HMs for CGD as monotherapy. Furthermore, experimental studies on the mechanism of action and the dose-response relationship of HMs are necessary to determine the optimal dosage.

Conclusions

Current evidence suggests that HMs may have the potential to enhance the treatment effect on CGD when combined with other treatments without serious adverse events. Since the overall quality of the studies included in this review was generally low, additional high-quality evidence is needed to draw a definite conclusion.

List Of Abbreviations

BBTT, Banxia Baizhu Tianma tang;
BYT, Buzhong Yiqi tang;
CGD, Cervicogenic dizziness;
CiNii, Citation Information by NII;
CENTRAL, Cochrane Central Register of Controlled Trials;
CGRP, Calcitonin gene-related peptide;
CNKI, China National Knowledge Infrastructure;
DBpia, Database Periodical Information Academic;
DXT, Dingxuan tang;
EMBASE, Excerpta Medica database;
ET, Endothelin;
Fib, Fibrinogen;
GGT, Guizhi Gegen tang;
GJT, Gegen Jieji tang;
GRADE, the Grading of Recommendations Assessment, Development, and Evaluation;
HM, Herbal medicine;
KISS, Korean studies Information Service System;
Declarations

Author contributions

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Funding

H.O. is supported by Kyung Hee University’s scholarship. S.S. and E.L. are supported by a grant from the National Research Foundation of Korea funded by the Korea government (Grant no.2020R1F1A1068808). E.L. and W.S.C. are supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI) funded by the Ministry of Health & Welfare, Republic of Korea (Grant no.HI20C1405). The funder played no role in the interpretation or publication of the study results.

Availability of data and materials

All data analysed during this study are included in this published article. The data supporting our findings are included within the manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

Acknowledgements

Not applicable.

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Figures
Records identified through database searching (n = 7,735)
- MEDLINE (n = 494); EMBASE (n = 2,345);
- CENTRAL (n = 1,018); KoreaMed (n = 82);
- KISS (n = 355); RISS (n = 268); NDSL (n = 721);
- KMbase (n = 290); DBpia (n = 217);
- CNKI (n = 1,925); CiNii (n = 20)

Additional records identified through other sources (n = 1)

Records after duplicates removed (n = 7,431)

Records screened (n = 7,431)

Records excluded (n = 6,765)

Full-text articles assessed for eligibility (n = 666)

Full-text articles excluded, with reasons (n = 649) listed as the following:
- Full-text unavailable (n = 17);
- Not clinical research (n = 31);
- Case report (n = 21);
- Not comparative study (n = 164);
- Nonrandomized controlled trial (n = 5);
- Not related to CGD (n = 258);
- Not related to intervention (n = 48);
- Not related to clinical question (n = 105)

Studies included in qualitative synthesis (n = 17)

Studies included in quantitative synthesis (n = 17)

Figure 1

PRISMA flow diagram of the literature screening and selection process. Abbreviations: CiNii, Citation Information by NII; CENTRAL, Cochrane Central Register of Controlled Trials; CGD, Cervicogenic dizziness; CNKI, China National Knowledge Infrastructure; DBpia, Database Periodical Information Academic; EMBASE, Excerpta Medica database; KISS, Korean Studies Information Service System; KMbase, Korean Medical Database; MEDLINE, Medical Literature Analysis and Retrieval System Online; NDSL, National Digital Science Library; RISS, Research Information Sharing Service
### Figure 2

Risk of bias summary for all included studies. The risk of bias was evaluated as "low," "high," or "some concerns", represented with the following symbols, respectively: "+", "−", and "?". Abbreviations: D, bias due to deviations from intended interventions; Me, bias in measurement of the outcome; Mi, bias due to missing outcome data; O, overall risk of bias; R, bias arising from the randomisation process; S, bias in the selection of the reported result.

| Study       | R | D | Mi | Me | S | O |
|-------------|---|---|----|----|---|---|
| Dai 2018    | + | - | -  | +  | + | + |
| Gao 2018    | ? | ? | ?  | +  | + | ? |
| Gu 2018     | + | - | +  | +  | + | + |
| Gu 2019     | ? | ? | +  | +  | + | ? |
| Hu 2019     | ? | ? | +  | ?  | + | ? |
| Ji 2016     | + | - | ?  | +  | ? | ? |
| Liu 2019    | ? | - | +  | +  | + | + |
| Lyu 2017    | ? | - | +  | +  | + | + |
| Pan 2019    | + | - | +  | +  | + | + |
| Qin 2012    | ? | ? | ?  | ?  | ? | ? |
| Qiu 2018    | ? | - | +  | +  | + | + |
| Shang 2016  | ? | - | ?  | ?  | ? | ? |
| Tan 2019    | + | ? | +  | ?  | ? | ? |
| Wang 2010   | + | - | -  | ?  | ? | ? |
| Yang 2018   | ? | - | +  | +  | + | ? |
| Yao 2018    | + | - | +  | +  | + | + |
| Zhu 2019    | ? | - | +  | +  | + | ? |
Figure 3

Funnel plot of the effect of HMs plus active controls on the overall function scores.
Supplementary Files

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