A Meta-Analysis of Migraine Treated with Banxia Baizhu Tianma Decoction

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Abstract

Objective Our objective was to systematically evaluate the efficacy and safety of Banxia Baizhu Tianma decoction in the treatment of migraine.

Methods The databases of China National Knowledge Infrastructure, VIP, WanFang, Chinese Biomedical Databases, PubMed, and EMBase were searched by computer, and randomized controlled trials that met the inclusion criteria were retrieved. The Cochrane bias risk assessment tool was used to evaluate the quality of the included studies. RevMan 5.3 software was used to conduct meta quantitative analysis of the included studies.

Results A total of 19 studies were included, with a total sample size of 1,635 cases, 821 cases in the treatment group and 814 cases in the control group. The results of meta-analysis showed that (1) the clinical effective rate of the single use of Banxia Baizhu Tianma decoction or western medicine combined with Banxia Baizhu Tianma decoction in treating migraine was better than that of western medicine alone (p < 0.001); (2) the improvement in cumulative number and days of vertigo in the treatment of migraine with Banxia Baizhu Tianma decoction was observed in the control group (p < 0.001). TSA results showed that Z-curve passed both the traditional threshold and Trial sequential analysis (TSA) threshold. In terms of adverse reactions, 55 cases were reported, including 12 cases in the treatment group and 43 cases in the control group, and no serious adverse reactions were found.

Conclusion Compared with the single use of western medicine therapy, the combination of Banxia Baizhu Tianma decoction and western medicine or the single use of Banxia Baizhu Tianma decoction could better improve the effective rate and showed good safety and low incidence of adverse reactions.
Introduction

Migraine is a primary neurovascular disease characterized by recurrent unilateral or bilateral severe throbbing pain in the head. When it attacks, it is often accompanied by the symptoms of nausea and vomiting, aggravated by acousto-optic stimulation, and relieved by rest. When migraine attacks, patients often cannot perform normal daily activities due to pain, which has a great negative impact on their quality of life and physical and mental health. According to statistics, the prevalence of migraine in adults worldwide is 15.3%, and migraine has become a common disease in humans. About 9.3% of adults in China have migraine, and women have more migraine than men.1-3 At present, it still lacks radical therapy for migraine, which is generally treated with herbs, mainly including acute attack treatment and remission prevention. Guidelines for the diagnosis and treatment of migraine in China indicate that the main recommended drugs in the acute phase are nonsteroidal anti-inflammatory drugs, such as acetaminophen and ibuprofen to achieve the rapid analgesic effect or vasoconstriction through drugs such as triptan and ergotamine to relieve migraine symptoms. During the remission period, commonly used drugs include calcium antagonists, β-blockers, antiepileptic drugs, antidepressants, etc.4 However, after long-term use of the above drugs, a series of adverse reactions such as fatigue, dizziness, drug-dependent headache, and gastrointestinal discomfort may occur, and a few patients may also have serious adverse reactions such as myocardial infarction and arrhythmia. In recent years, good results have been achieved in migraine intervention with Chinese herbs, especially in reducing the use of western medicine, thereby reducing adverse drug reactions. Banxia Baizhu Tianma decoction can dissolve phlegm, calm wind, strengthen the spleen, and dispel dampness. Clinical practices have proved that this prescription has unique advantages in the treatment of migraine in China,4 the age, gender, and course of disease of patients diagnosed with migraine by Western medicine are not limited.

Interventions

Intervention of treatment group included single use of Banxia Baizhu Tianma decoction or Banxia Baizhu Tianma decoction combined with conventional western medicine treatment. Control group intervention included conventional western medicine.

Outcome Indicators

The primary outcome indicators in this study were clinical efficacy and the times of occurrence of adverse reactions. Clinical efficacy refers to the relevant requirements and standards in the Guidelines for Clinical Study of New Drugs in Chinese Medicine5: Cured: headache and concomitant symptoms were completely terminated; significant effect: the intensity of headache was reduced by two grades compared with that before treatment, the number of headache attacks was reduced by ≥ 2/3 compared with that before treatment, or the duration of pain was reduced by ≥ 2/3 compared with that before treatment; effect: the intensity of headache was reduced by one grade, the headache duration was reduced by < 2/3, or the interval between headache episodes was prolonged; ineffective: pain intensity decreased by < 1 grade, pain duration decreased by < 1/3, or headache intensity increased and duration prolonged.

Clinical effective rate = (cured + significantly effective + effective)/total sample size × 100%

Secondary outcome indicators were headache frequency, headache duration, cumulative number of dizziness, cumulative time of dizziness, plasma endothelin-1 (ET-1), and nitric oxide.

Exclusion Criteria

Exclusion criteria were (1) the literature not published in Chinese or English; (2) the control scheme designed as self-controlled randomized trial; (3) studies with absent outcome indicators; and (4) repeatedly published or data-repeated studies.

Materials and Methods

Inclusion Criteria

Type of the Study

This was a randomized controlled trial of Banxia Baizhu Tianma decoction in the treatment of migraine published at home and abroad.

Study Object

According to the Diagnostic Criteria for Migraine 2004 (International Classification of Headache Disorders 2nd edition [ICHD-2]),7 Diagnostic Criteria for Migraine 2013 (ICHD-3)8 formulated by the International Headache Association, and the Guidelines for the Prevention and Treatment of Migraine in China,4 the age, gender, and course of disease of patients diagnosed with migraine by Western medicine are not limited.

Literature Retrieval

The following six databases were searched by computer: PubMed, EMBase, Chinese Biomedical Literature Database, China Science and Technology Journal Database, Chinese Academic Journals Index Database, and Wanfang Medical Database. The search time was set to June 13, 2022. The search terms were migraine, migraine disorder, and Banxia Baizhu Tianma decoction. Taking PubMed as an example, the specific search strategies were as follows: #1 Search migraine disorders [MeSH Terms]; #2 Search migraine disorders [-Title/Abstract]; #3 Search disorder, migraine [Title/Abstract] OR migraine [Title/Abstract] OR migraine disorder [-Title/Abstract] OR disorders, migraine [Title/Abstract]; #4 Search Banxia Baizhu Tianma decoction [MeSH Terms]; #5 #1 OR #2 OR #3; #6 #4 AND #5.
Literature Screening and Data Extraction
The retrieved articles were imported into NoteExpress reference management software by two researchers, duplicate articles were eliminated by duplicate search function, the titles and abstracts of the documents were read according to the established screening criteria, and the articles were preliminarily screened to exclude obviously nonconforming ones. The full text of the articles that may be included was further read to reconfirm whether they comply with the inclusion criteria. In case of disagreement in the literature screening process, it can be resolved through joint discussion or consultation with relevant experts. Data extraction was performed by using a unified data extraction form developed using Microsoft Excel tables, containing the following contents: (1) general information included in the study: author, date of publication, diagnostic criteria, demographic baseline, interventions, number and performance of cases with adverse reactions, and outcome indicators; (2) literature quality evaluation: it included randomized method, allocation concealment method, blind method, follow-up bias, and reporting bias.

Risk Assessment of Bias Included in the Study
According to the evaluation criteria established in the Cochrane System Evaluation Manual, the quality of included randomized controlled trials was systematically evaluated by using the Cochrane Bias Risk Assessment Tool. The evaluation contents included (1) random sequence generation method; (2) allocation concealment (whether the allocation is correctly concealed); (3) implementation bias (whether the investigator and subjects are blinded); (4) measurement bias (whether the study evaluator is blinded); (5) follow-up bias (whether the study results are complete); (6) report bias (whether selective reporting exists); and (7) other biases. Each evaluation content was judged by “low risk,” “high risk,” and “unclear risk.”

Statistical Methods
The extracted data were entered into the RevMan 5.3 software for processing. The effect analysis statistics were selected as follows: the risk ratio (RR) was used for the counting data, and the mean difference (MD) or standardized mean difference (SMD) was used for the measurement data as the effect analysis statistics (MD was selected when the units of measure were the same and SMD was selected when the units of measure were different). The confidence interval (CI) was set to 95%, and each effect measure provided its effect value. The results of the study were assessed for heterogeneity between groups using $X^2$ test analysis, and the results were quantified by using $I^2$. When $P > 0.1$ and $I^2 \leq 50\%$, the heterogeneity between studies was small. Therefore, the fixed effect model was used for systematic evaluation and analysis. When $P \leq 0.1$ and $I^2 \geq 50\%$, it suggested that the heterogeneity between studies was large, and the cause of heterogeneity could be explored by subgroup analysis or sensitivity analysis. When the studies with obvious clinical heterogeneity had been excluded, the random effect model was selected for combination.

Results

Literature Search Results
A total of 199 relevant articles were retrieved from all databases and imported into NoteExpress literature management software, and 75 duplicate articles were removed. According to the inclusion and exclusion criteria, 33 articles were retained after rescreening by reading the title and abstracts of the articles, and the full texts were downloaded and read. Finally, a total of 19 articles were included in this study.

Basic Characteristics of the Included Literature
Finally, 19 randomized controlled trials were included in this study, with a total of 1,635 patients. The number of patients in the treatment group and the control group was 821 and 814, respectively. The maximum sample size $n = 80$ and the minimum sample size $n = 13$ were included in the 19 studies. The baseline levels of the treatment group and the control group were statistically analyzed, and there was no significant difference ($P > 0.05$), which was comparable. The basic characteristics of the included articles are shown in Table 1.

Quality Assessment of Included Literature
In terms of random sequence generation methods, two studies were randomized according to different treatment methods and the order of consultation, so they were labeled high risk. Eight studies only mentioned “randomized,” but the specific randomization method was unknown, so it was marked as unclear risk. The remaining nine studies were labeled low risk using the random number counter method. None of the 19 studies specified randomization concealment, blinding, and the presence or absence of other biases, and all of them were labeled as unclear risk. None of the 19 studies had missing outcome data or selective reporting and were labeled as low risk. The literature quality evaluation is shown in Fig. 1.

Publication Bias Analysis
Funnel plots for clinical effective rate were prepared by using RevMan 5.3 software. The results were mostly distributed at the top of the plots and evenly distributed on both sides, indicating that the publication bias were small. The results are shown in Fig. 2.

Meta-Analysis Results
A total of 19 articles of randomized controlled trials were included in this study. Data processing and meta-analysis were performed in groups according to the differences in control measures.

Clinical Effective Rate
A total of 17 articles reported the clinical efficacy. Seventeen studies were tested for heterogeneity, and the results were $p = 0.35$ and $I^2 = 9\%$, indicating that the heterogeneity was small. Therefore, the fixed effect model was used for systematic evaluation and analysis. The results showed
<table>
<thead>
<tr>
<th>Included study</th>
<th>n(T/C)</th>
<th>Course of disease (T/C, years)</th>
<th>Course of treatment (T/C,d)</th>
<th>Therapeutic medicine</th>
<th>Outcome</th>
<th>Indication</th>
<th>Adverse reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhang 2007 ¹¹</td>
<td>80/80</td>
<td>8.15 ± 7.54/8.12 ± 7.59</td>
<td>−/−</td>
<td>Banxia Baizhu Tianma decoction, 1 dose, bid</td>
<td></td>
<td>General therapy in western medicine</td>
<td>①</td>
</tr>
<tr>
<td>Pu et al 2008 ¹²</td>
<td>45/45</td>
<td>6.2/5.8</td>
<td>28/28</td>
<td>Supplemented Banxia Baizhu Tianma decoction, 1 dose, bid</td>
<td></td>
<td>Flunarizine hydrochloride capsules, 5 mg, qd</td>
<td>①</td>
</tr>
<tr>
<td>Sun et al 2014 ¹³</td>
<td>30/30</td>
<td>0.97 ± 0.38/0.9 ± 0.3</td>
<td>7/7</td>
<td>Modified Banxia Baizhu Tianma decoction, 1 dose, bid</td>
<td></td>
<td>Flunarizine hydrochloride capsules, 5 mg, qd</td>
<td>①</td>
</tr>
<tr>
<td>Zhang et al 2014 ¹⁴</td>
<td>53/50</td>
<td>4.8/5.2</td>
<td>60/45</td>
<td>Modified Banxia Baizhu Tianma decoction, 1 dose, bid + flunarizine hydrochloride capsules, 10 mg, qd</td>
<td></td>
<td>Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>①</td>
</tr>
<tr>
<td>Liu 2015 ¹⁵</td>
<td>77/76</td>
<td>6.8 ± 3.4/6.7 ± 3.5</td>
<td>30/30</td>
<td>Modified Banxia Baizhu Tianma decoction, 1 dose, bid + flunarizine hydrochloride capsules, 10 mg, qd</td>
<td></td>
<td>Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>①</td>
</tr>
<tr>
<td>Ou et al 2016 ¹⁶</td>
<td>45/45</td>
<td>8.6 ± 5.5/8.6 ± 6.0</td>
<td>42/42</td>
<td>Supplemented Banxia Baizhu Tianma decoction</td>
<td></td>
<td>Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>①②③④</td>
</tr>
<tr>
<td>Wang et al 2016 ¹⁷</td>
<td>60/60</td>
<td>0.05 ± 2/0.06 ± 2.33</td>
<td>42/42</td>
<td>Modified Banxia Baizhu Tianma decoction, 1 dose, bid + flunarizine hydrochloride capsules, 10 mg, qd</td>
<td></td>
<td>Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>①</td>
</tr>
<tr>
<td>Guan et al 2016 ¹⁸</td>
<td>45/45</td>
<td>10.9 ± 4.4/10.9 ± 4.4</td>
<td>15/15</td>
<td>Banxia Baizhu Tianma decoction, 1 dose, bid</td>
<td></td>
<td>Flunarizine hydrochloride capsules, 10 mg, bid</td>
<td>①</td>
</tr>
<tr>
<td>Kang et al 2017 ¹⁹</td>
<td>27/27</td>
<td>−/−</td>
<td>60/3</td>
<td>Banxia Baizhu Tianma decoction, 1 dose, bid</td>
<td></td>
<td>Betahistine mesylate tablets, 12 mg, tid</td>
<td>①②③</td>
</tr>
<tr>
<td>Liu 2018 ²⁰</td>
<td>42/41</td>
<td>−/−</td>
<td>15/15</td>
<td>Banxia Baizhu Tianma decoction, 1 dose, bid + flunarizine hydrochloride capsules, 10 mg, qd</td>
<td></td>
<td>Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>①</td>
</tr>
<tr>
<td>Wang 2018 ²¹</td>
<td>23/23</td>
<td>−/−</td>
<td>−/−</td>
<td>Supplemented Banxia Baizhu Tianma decoction, 1 dose, bid</td>
<td></td>
<td>Nimodipine, 20 mg, tid</td>
<td>①</td>
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<tr>
<td>Liu et al 2019 ²²</td>
<td>36/36</td>
<td>1.5–33.5/0.58–31.2</td>
<td>14/14</td>
<td>Supplemented Banxia Baizhu Tianma decoction, 1 dose, bid</td>
<td></td>
<td>Flunarizine hydrochloride capsules, 5 mg, qd</td>
<td>①</td>
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<tr>
<td>Gao et al 2019 ²³</td>
<td>35/33</td>
<td>6.89 ± 2.07/6.35 ± 14.58</td>
<td>28/28</td>
<td>Sheng Qi Banxia Baizhu Tianma decoction, 1 dose, bid</td>
<td></td>
<td>Flunarizine hydrochloride tablets, 10 mg, qd</td>
<td>①</td>
</tr>
</tbody>
</table>

(Continued)
Table 1 (Continued)

<table>
<thead>
<tr>
<th>Included study</th>
<th>n(T/C)</th>
<th>Course of disease (T/C, years)</th>
<th>Course of treatment (T/C,d)</th>
<th>Therapeutic medicine</th>
<th>Outcome</th>
<th>Adverse reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li 2020&lt;sup&gt;24&lt;/sup&gt;</td>
<td>42/42</td>
<td>5.27 ± 0.43/5.21 ± 0.91</td>
<td>14/14</td>
<td>Banxia Baizhu Tianma decoction, 1 dose, bid + Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>①⑥⑦</td>
</tr>
<tr>
<td>Zheng 2020&lt;sup&gt;25&lt;/sup&gt;</td>
<td>43/43</td>
<td>11.04 ± 2.19/10.72 ± 2.54</td>
<td>42/42</td>
<td>Supplemented Banxia Baizhu Tianma decoction, 1 dose, bid</td>
<td>Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>①②③</td>
</tr>
<tr>
<td>Li 2020&lt;sup&gt;5&lt;/sup&gt;</td>
<td>13/13</td>
<td>30.67 ± 6.41/29.58 ± 5.32</td>
<td>14/3</td>
<td>Banxia Baizhu Tianma decoction, 1 dose, bid + Betahistine Mesylate tablets, 12 mg, tid</td>
<td>Betahistine Mesylate tablets, 12 mg, tid</td>
<td>④⑤</td>
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<td>Yan 2020&lt;sup&gt;26&lt;/sup&gt;</td>
<td>40/40</td>
<td>–/–</td>
<td>21/21</td>
<td>Banxia Baizhu Tianma decoction, 1 dose, bid</td>
<td>Flunarizine hydrochloride capsules, 5 mg, bid</td>
<td>①</td>
</tr>
<tr>
<td>Pan 2021&lt;sup&gt;27&lt;/sup&gt;</td>
<td>25/25</td>
<td>–/–</td>
<td>14/14</td>
<td>Banxia Baizhu Tianma decoction, 1 dose, bid + Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>①</td>
</tr>
<tr>
<td>Yang et al 2022&lt;sup&gt;28&lt;/sup&gt;</td>
<td>60/60</td>
<td>–/–</td>
<td>14/14</td>
<td>Supplemented Banxia Baizhu Tianma decoction, 1 dose, bid + Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>Flunarizine hydrochloride capsules, 10 mg, qd</td>
<td>①</td>
</tr>
</tbody>
</table>

Notes: T: treatment group; C: control group; –: not mentioned. ① clinical effective rate; ② ET-1; ③ NO; ④ the cumulative number of vertigo; ⑤ the cumulative time of vertigo; ⑥ frequency of headache; ⑦ duration of headache.
that the clinical efficiency of the observation group was significantly better than that of the control group, and the therapeutic effects were significantly different ($RR = 1.27$, 95% CI: 1.21, 1.33, $p < 0.001$), as shown in ►Fig. 3.

Cumulative Number and Time of Vertigo

Two articles5,19 reported the cumulative number of vertigo and the improvement in the cumulative days of dizziness in the treatment of migraine with Banxia Baizhu Tianma decoction compared with Betahistine Mesylate tablets. The heterogeneity test results were $p = 0.90$, $I^2 = 0$, indicating that the heterogeneity was small. The fixed effect model was used for the combined effect. The results showed that Banxia Baizhu Tianma decoction was significantly better than the control group in improving the cumulative times and days of dizziness in migraine patients, and the effects were significantly different ($MD = -3.24$, 95% CI: $-4.57$, $-1.90$, $p < 0.001$), ($MD = -3.84$, 95% CI: $-6.06$, $-1.62$, $p < 0.001$), as shown in ◄Figs. 4 and 5.

Sequential Analysis of Test

TSA V0.9 software was used to perform sequential analysis on 17 articles11–18,20–28 that reported clinical efficacy. The probability of type I error and type II error were set to $\alpha = 0.05$ and $\beta = 0.2$, respectively. The sample size was taken as the expected information score, and curve B (Z value) passed through straight line C (traditional boundary) and curve A (TSA boundary) at the same time, as shown in ◄Fig. 6. Therefore, Banxia Baizhu Tianma decoction could improve the clinical efficacy for migraine and the evidence was accurate.

The TSA V0.9 software was used for punishment statistics analysis. Set type I error probability $\alpha = 0.05$ and penalty value $\lambda = 2$. The punishment statistics chart is shown in ◄Fig. 7. The Z-value curve (green curve) after punishment exceeded the traditional limit, so it was confirmed that the effective rate of the observation group was better than that of the control group.

Safety Analysis

As shown in ◄Table 2, a total of 10 studies5,15,16,18–22,24,27 reported adverse reactions, of which 2 studies21,27 did not specifically describe the specific manifestations and the
remaining 7 studies reported the clinical manifestations of adverse reactions, as shown in Table 2.

### Discussion

Migraine is a common clinical disabling headache disease. The disease has a repeated course and is difficult to cure. It often develops into a chronic disease and affects the quality of life of patients, causing serious harm to their health. Clinically, active measures can be taken to reduce the degree and frequency of headache attacks and relieve the accompanying symptoms. At present, western drugs for migraine mainly include analgesics (such as nonsteroidal anti-inflammatory drugs and opioids), calcium channel blockers, β receptor blockers, etc. Flunarizine hydrochloride is a commonly used drug in the clinical treatment of migraine. It is widely used in the preventive treatment of migraine and can relieve migraine by inhibiting the content of nitric oxide and calcitonin gene-related peptide, but it is often accompanied by a variety of adverse reactions, such as fatigue, lethargy, depression, etc. Betahistine methanesulfonate is a drug used to treat vertigo and balance dysfunction, which can improve cerebral blood circulation and has a certain therapeutic effect on vestibular migraine.
Migraine can be classified as “head wind” and “headache” in TCM, the pathogenesis of which is often divided into two categories: external contraction and internal injuries. Migraine can be caused by obstruction or insufficiency of qi and blood resulting from exogenous six abnormal climatic factors, emotional disorders, irregular diet and insufficient natural endowment, as well as obstruction of brain collateral or brain collateral dystrophy. Academician Yongyan Wang summarized that the disease was mainly located in the liver, and blood stasis and wind pathogens were the key factors for the onset of the disease. He pointed that wind pathogens induced phlegm and blood stasis

Table 2 Occurrence of adverse reactions

<table>
<thead>
<tr>
<th>Author Year</th>
<th>Total number of cases with adverse reactions (T/C)</th>
<th>Number of cases with adverse reactions (T/C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dry mouth</td>
<td>Gastric discomfort</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tiredness and drowsiness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insomnia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extrapyramidal symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Transient transaminase increased</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rash</td>
</tr>
<tr>
<td>Li 2020&lt;sup&gt;5&lt;/sup&gt;</td>
<td>1/4</td>
<td>0/1</td>
</tr>
<tr>
<td>Liu 2015&lt;sup&gt;15&lt;/sup&gt;</td>
<td>2/9</td>
<td>–</td>
</tr>
<tr>
<td>Ou et al 2016&lt;sup&gt;16&lt;/sup&gt;</td>
<td>3/5</td>
<td>3/0</td>
</tr>
<tr>
<td>Guan et al 2016&lt;sup&gt;18&lt;/sup&gt;</td>
<td>2/8</td>
<td>–</td>
</tr>
<tr>
<td>Kang et al 2017&lt;sup&gt;19&lt;/sup&gt;</td>
<td>0/2</td>
<td>0/1</td>
</tr>
<tr>
<td>Liu 2018&lt;sup&gt;20&lt;/sup&gt;</td>
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<td>Pan 2021&lt;sup&gt;27&lt;/sup&gt;</td>
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</table>

Fig. 7 Punishment statistical chart
which would further disturb the clear orifices, and qi and blood would be disturbed and result in acute attacks. Therefore, it emphasizes the simultaneous use of the method of calming the liver and calming the wind and the method of removing phlegm and dredging collaterals in clinical treatment. 31 Banxia Baizhu Tianma decoction is originated from Medical Revelations, which consists of eight Chinese herbs, namely Banxia (Pinelliae Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Tianma (Gastrodiae Rhizoma), Fuling (Poria), Juhong (Exocarpium Citri Rubrum), Dazao (Jujubae Fructus), and Shengjiang (Zingiberis Rhizoma Recens). Based on Erchen Decoction, Tianma (Gastrodiae Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), and Dazao (Jujubae Fructus) are added. In the prescription, the Banxia (Pinelliae Rhizoma) and Juhong (Exocarpium Citri Rubrum) are compatible, which can dry dampness and disperse phlegm, regulate qi, and harmonize the middle energizer, embodying the method of strengthening spleen and stomach to eliminate phlegm and dampness. Tianma (Gastrodiae Rhizoma) often enters the liver meridian and is effective for calming the liver, resolving phlegm and quenching wind, which is an important herb for treating wind-phlegm headache. Fuling (Poria) has the functions of invigorating spleen, resolving dampness. Baizhu (Atractylodis Macrocephalae Rhizoma) has the effects of invigorating spleen and drying dampness, and the combination of the two can promote the transformation function of the spleen and jointly treat the root of phlegm. Dazao (Jujubae Fructus) regulates the spleen and stomach, and Gancao (Glycyrrhizae Radix et Rhizoma) harmonizes various herbs. Combined with other herbs, it has the effects of resolving phlegm, calming wind, invigorating the spleen, and dispelling dampness and is suitable for treating wind-phlegm syndrome of migraine. Modern pharmacology shows that Banxia Baizhu Tianma decoction has the effects of regulating the levels of nitric oxide, endothelin, and angiotensin II. 32 In addition, Banxia Baizhu Tianma decoction can reduce the levels of norepinephrine and serotonin in the peripheral plasma by regulating the gene expression of serotonin 1B/1D receptor in the brain tissue of migraine rats, 33,34 thus achieving the therapeutic effects on migraine. Meta-analysis showed that the clinical efficacy of the single use of Banxia Baizhu Tianma decoction or combined with western medicine was superior to that of single use of western medicine, which could reduce the intensity of headache, the frequency of attack and the duration of pain. TSA analysis showed that the efficacy of Banxia Baizhu Tianma decoction in treating migraine was confirmed and the sample size required for meta-analysis was reached. In addition, most of the included studies did not appear serious adverse reactions. Therefore, in the existing research reports, no serious adverse reactions have been found in the treatment of migraine with the single use of Banxia Baizhu Tianma decoction or Banxia Baizhu Tianma decoction combined with western medicine, and a few patients may have mild adverse reactions. However, due to the small sample size involved in relevant studies and the lack of reporting of long-term follow-up results, it is still necessary to further evaluate its safety with rigorous design, comprehensive evaluation indicators, and long-term follow-up studies.

There were some limitations in this study: (1) some included articles did not specify the random protocol or the bias of the random protocol, resulting in the possible publication bias of the analysis results; (2) it is difficult to implement the blind method due to the oral administration of Chinese medicine decoction in the intervention; (3) the main outcome indicators, including headache intensity, pain duration, and headache frequency, are subjective to some extent, which makes the demonstration strength slightly insufficient; (4) only some studies mentioned adverse reactions, and no long-term follow-up and reporting were conducted in all studies, making it difficult to accurately evaluate the safety of treatment. In addition, summarizing the 19 randomized controlled trials included in this study, there are still deficiencies in clinical studies, such as the oversimplified description of adverse reactions in some studies and incomplete presentation of case data. It is recommended that follow-up clinical studies should adopt the correct randomization method and make specific reports and completely record and report the subject's case data. Adverse reactions should be described in detail, and the follow-up treatment should be reported so as to more objectively evaluate the safety of the treatment regimen. In addition, large sample, multicenter combined clinical trials should be conducted as far as possible.

Conclusion
Banxia Baizhu Tianma decoction combined with Western medicine or single use of Banxia Baizhu Tianma decoction can improve the clinical efficacy without serious adverse reactions. Given the limitations of this study and the methodological design deficiencies of the included studies, high-quality randomized controlled trials with large sample size, rigorous and standardized design, comprehensive evaluation, and reporting of long-term follow-up results are still needed to verify and obtain the support of higher evidence-based medical evidence.

CRediT Authorship Contribution Statement
Xueyan Chen: Conceptualization, data curation, software, and writing original draft. Zheyan Liu: Data curation, formal analysis, writing original draft. Jie Zhang: Investigation, data curation, project administration, and writing. Juanjuan Chen: Investigation, software and methodology. Qiude Qin: Acquisition, supervision, and writing-review & editing. Feng Jiang: Writing-review & editing.

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Conflict of Interest
The authors declare no conflict of interest.
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