SYSTEMATIC REVIEW & META ANALYSIS

Systematic Review and Meta-analysis on the Efficacy and Safety of Xuefu Zhuyu Oral Liquid (血府逐瘀口服液) in the Treatment of Migraine

CAO Jing (曹 竟)[1,2], LYU Jian (吕 健)[2], XIE Yan-ming (谢雁鸣)[1]

1. Institute of Basic Research in Clinical Medicine, China Academy of Chinese Medical Sciences, Beijing 100700, China
2. Xiyuan Hospital, China Academy of Chinese Medical Sciences, Beijing 100091, China

Correspondence to: XIE Yan-ming, E-mail: ktzu2018@163.com

Supported by: 2021 Qihuang Scholars Support Project of National Administration of Traditional Chinese Medicine (National Letter of TCM Education [2022] No.6)

ABSTRACT **Objective:** To systematically evaluate the efficacy and safety of Xuefu Zhuyu Oral Liquid (血府逐瘀口服液) in the treatment of migraine. **Methods:** All randomized controlled trials (RCTs) on the treatment of migraine with Xuefu Zhuyu Oral Liquid were screened out by systematically searching Cochrane Library, PubMed, Embase, Web of Science, VIP, Wanfang, CNKI and CBM database from database establishment to March 2023. Literature screening was conducted strictly according to inclusion and exclusion criteria, and the quality of the finally included RCTs was evaluated according to the Cochrane Handbook. All data analyses were completed using RevMan 5.4 software provided by the Cochrane Collaboration. **Results:** A total of 8 RCTs involving 706 patients were included. Meta-analysis showed that Xuefu Zhuyu Oral Liquid alone (RR=1.22, 95%CI [1.11, 1.33], *P*<0.0001) or combined with conventional treatment (RR=1.19, 95%CI [1.11, 1.28], *P*<0.0001) was superior to conventional treatment alone in improving the severity of headache attacks and reducing recurrence. Three studies mentioned mild adverse reactions in individual patients during the treatment process, such as transient diarrhea, lethargy, etc., which were not directly related to Xuefu Zhuyu Oral Liquid. **Conclusion:** Based on the existing data and meta-analysis results, Xuefu Zhuyu Oral Liquid alone or combined with conventional treatment can improve the total effective rate of migraine treatment, alleviate headache symptoms, reduce recurrence and adverse events. In the future, large-scale and high-quality original studies are needed to further verify the efficacy and safety of Xuefu Zhuyu Oral Liquid in the treatment of migraine, and provide a reference for the clinical medication of migraine.

KEYWORDS Chinese patent medicine; Xuefu Zhuyu Oral Liquid; Migraine; Meta-analysis; Systematic review

Migraine is characterized by recurrent, unilateral or bilateral throbbing, severe headache, lasting 4–72 hours.[1] The onset of this disease is often accompanied by autonomic nervous system dysfunction such as photophobia, phonophobia, nausea, and vomiting, and is characterized by familial inheritance and a high recurrence rate.[2] According to a meta-analysis of the 2016 Global Burden of Disease Survey,[3] approximately one billion people worldwide suffer from migraine, which is the sixth most common clinical condition and the second most disabling disease after osphyalgia, placing a significant economic and psychological burden on patients and society. In recent years, the incidence of migraine has increased significantly with the aging of the Chinese population, which greatly impacts patients' psychological state and quality of life.

However, there is still no definite conclusion about the pathogenesis of migraine. The vascular theory suggests that constriction of the blood vessels inside the skull leads to migraine. The trigeminovascular reflex theory suggests that the pain signals from the trigeminal nerve are transmitted via axons to the trigeminal vascular

(C)1994-2024 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net

system, which in turn conducts to the cerebral cortex to produce pain.[4] Most studies have concluded that treating migraine as a recurrent disease, aims to reduce the frequency and severity of headache attacks to improve the quality of life and restore social function,[5,6] but not to obtain a cure. Currently, the main drugs available for the treatment of migraine are the specific drugs of the triptans and nonspecific analgesics, such as opioids and non-steroidal anti-inflammatory drugs (NSAIDs). Triptans are the preferred drugs for acute migraine attacks. They have adverse effects such as palpitations, irritability, vasoconstriction, nausea, vomiting, and are still resistant to them in about 40% of patients.[7] Opioids[8] and NSAIDs[9] can cause serious side effects, such as respiratory depression, anaphylactic shock, gastrointestinal bleeding, and arrhythmias. Currently, the range of drugs available for migraine is limited, and all of them have certain adverse reactions, which are challenging to meet the actual needs of patients. Therefore, there is an urgent need to seek new therapies with significant efficacy and high safety.

The classical Chinese medicine formulas and their modified dosage form have shown promising clinical effects on migraines.[10] Xuefu Zhuyu Oral Liquid (血府逐瘀口服液) originated from Xuefu Zhuyu Decoction (血府逐瘀汤) of Wang Qingren in the Qing Dynasty, which consists of 11 herbs, including Taoren (*Peach Kernel*, 桃仁), Honghua (*Safflower*, 红花), Zhiqiao (*Fructus Aurantii*, 枳壳), Danggui (*Angelica*, 当归), Shengdihuang (*Radix Rehmanniae*, 生地黄), Chaihu (*Bupleurum*, 柴胡), Chuanxiong (*Chuanxiong Rhizoma*, 川芎), Gancao (*Licorice*, 甘草), Shaoyao (*Paeonia Lactiflora*, 赤芍), Jiegeng (*Platycodon Grandiflorum*, 桔梗), and Niuxi (*Achyranthes*, 牛膝).[11,12] Formulated with a large amount of ingredients that promote blood circulation, remove blood stasis, and unblock collaterals, it can treat various types of headaches, such as migraine, trigeminal headache and tension headache, which plays a role in promoting qi-relieving pain, activating blood and removing blood stasis. However, there is no systematic evaluation on the treatment of migraine with Xuefu Zhuyu Oral Liquid. This study systematically compiled the published randomized controlled trials on the treatment of migraine with Xuefu Zhuyu Oral Liquid and conducted a meta-analysis to investigate the effectiveness and safety of Xuefu Zhuyu Oral Liquid in treating migraine, in order to provide a reference for the clinical medication of migraine.

MATERIALS AND METHODS

Inclusion Criteria

The type of study was a published randomized controlled trial (RCT) in English and Chinese of Xuefu Zhuyu Oral Liquid in patients with a precise diagnosis of migraine, regardless of whether specific diagnostic criteria were given in the study, and regardless of the age, gender, duration of disease and race of the patients. The intervention measures in the experimental group were Xuefu Zhuyu Oral Liquid alone or Xuefu Zhuyu Oral Liquid combined with conventional treatment in the control group (dosing, method, and duration are not limited). The intervention measures in the control group were conventional treatment (referring to the preventive treatment methods in the 2016 *Chinese Guidelines for the Prevention and Treatment of Migraines*).[13] Commonly medicines include flunarizine hydrochloride capsules, nimodipine tablets, etc. were used. The results of each study were converted into binary variables, where ineffective was defined as ineffective, effective included three levels of "cured", "markedly effective", and "effective". The overall clinical effective rate was used as the primary outcome measure, calculated as (number of cured + markedly effective + effective cases)/total number of cases ×100%.

Exclusion Criteria

① The study subjects did not meet the diagnostic criteria for migraine; ② The intervention measures in the control group included other TCM adjunctive therapies such as acupuncture, auricular acupuncture, massage, etc; ③ If there is data duplication between two papers, the study with the most complete data would be retained; ④ The type of study did not match, such as literature review, animal experiments, or observational studies; ⑤ Studies for which the full text was not available.

Retrieval Strategy

All randomized controlled trials (RCTs) on the treatment of migraine with Xuefu Zhuyu Oral Liquid

(C)1994-2024 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net

were screened out by systematically searching Cochrane Library, PubMed, Embase, Web of Science, VIP, Wanfang, CNKI and CBM database from database establishment to March 2023. The search strategy was a combination of subject terms and free words. Search terms were "Xuefu Zhuyu oral solution"(#1), "Xuefu Zhuyu oral liquid"(#2), "migraine"(#3), "hemicrania"(#4), "cephalagra"(#5), "headaches"(#6), "randomized controlled trial"(#7), and "clinical observation"(#8). The English search formula was (#1 OR #2) AND(#3 OR #4 OR #5 OR #6) AND(#7 OR #8).

Study Selection and Data Extraction

Two researchers independently screened the literature based on the inclusion and exclusion criteria mentioned above. Firstly, all the retrieved literature was imported into Note Express for deduplication. Then, the researchers read the titles and abstracts of the literature for preliminary screening and finally eliminated all unqualified studies by reading the full text carefully. If there is a disagreement between two researchers, the third researcher participated in the decision. A data extraction table was created using Excel and Note Express, with extracted information mainly including the first author, year of publication, study subjects' baseline characteristics, literature quality, diagnostic criteria, intervention measures and outcome indicators.

Literature Quality Evaluation

Based on the bias risk assessment tool recommended by the Cochrane Collaboration (RevMan 5.4), two researchers evaluated the bias risk of RCTs from seven aspects, mainly from the random method, allocation concealment, blind implementation of participants and researchers, blind implementation of outcome evaluators, completeness of outcome data, selective reporting of study results, and other sources of bias. The quality of the included literature was assessed by comprehensively evaluating the bias risk as "low risk" "uncertain risk" or "high risk". If there is disagreement between two researchers, the third researcher participated in the discussion and judgment.

Statistical Analysis

This study used RevMan 5.4, provided by the Cochrane Collaboration to analyze all data. As a binary variable, clinical total effectiveness was evaluated by relative risk (RR) as an evaluation index, and 95% confidence interval (CI) as the interval estimation. Heterogeneity testing was performed between groups. A fixed-effect model was applied to analyze the data if $P \geqslant 0.1$ and $I^2 \leqslant 50\%$, indicating good homogeneity between the data. Conversely, if there is high heterogeneity between the data ($P<0.1$, $I^2>50\%$), subgroup analysis or sensitivity analysis was conducted. Studies with high heterogeneity were excluded, and a random-effect model was applied to combine the effect sizes for meta-analysis.

RESULTS

Literature Search Results

According to the search criteria mentioned above, 51 relevant articles (50 in Chinese and 1 in English) were initially retrieved from eight databases, including 1 from Cochrane Library, 13 from CNKI, 15 from Wanfang, 10 from VIP, 12 from CBM database, and no relevant papers from Web of Science, PubMed and Embase. The duplicate literature was eliminated by checking the above 51 articles, and 31 duplicates were removed. According to the inclusion and exclusion criteria, 12 unqualified studies were finally eliminated by carefully reading the abstracts and full texts. Consequently, only 8[14-21] Chinese articles were included. The basic information was extracted, including the first author, year of publication, treatment course, outcome indicators, sample size and intervention measures. The detailed screening processing was summarized in Figure 1.

Basic Characteristics of the Included Studies

The 8 articles finally included in the meta-analysis were all in Chinese, and 4 of them[17-19,21] described that the baseline was comparable between the experimental and control groups. The subjects of all 8 studies met the diagnostic criteria for migraine. A total of 706 cases were included, including 362 cases in the experimental group and 344 cases in the control group, with the largest sample size of 132 cases and the smallest of 40 cases. According to the different interventions in the experimental group, the studies were divided into two subgroups for analysis: Xuefu Zhuyu Oral Liquid alone and Xuefu Zhuyu Oral Liquid combined with conventional treatment. The

(C)1994-2024 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net

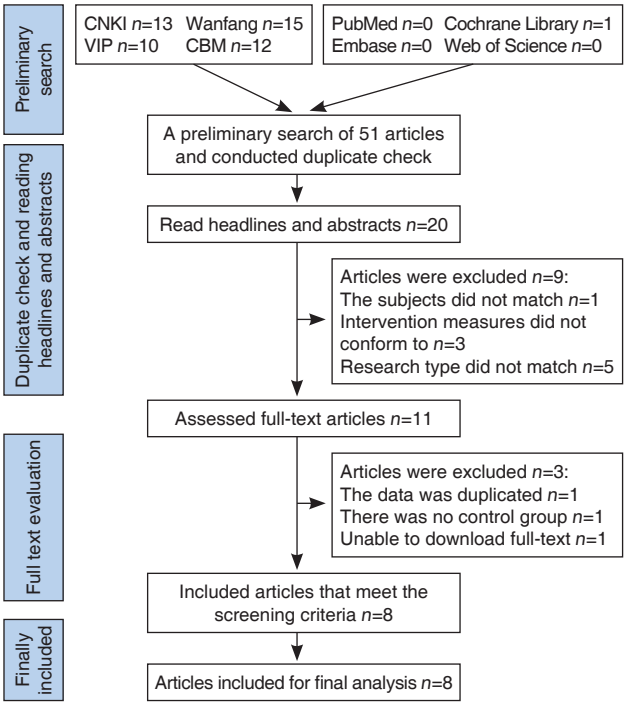


Figure 1. Article Screening Flow Diagram

former included 3 studies[14,16,18] and the latter included 5 studies[15,17,19-21]. See Table 1 for details.

Results of Quality Evaluation

All 8 articles included in the meta-analysis were RCTs. In terms of randomization sequence, all studies only mentioned the word "random," without specifying the specific method of random allocation, and thus were evaluated as uncertain risk of bias. None of the 8 studies reported whether allocation concealment and blinding were implemented, thus being assessed as uncertain risk of bias. There were no lost cases in all studies and complete data were reported. No selective publications or other biased sources were found, leading to a low risk of bias assessment. See Figure 2 and Figure 3 for the quality evaluation results of the included literature.

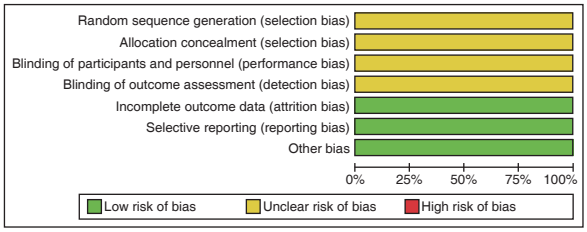


Figure 2. Percentage of Projects at the Risk of Bias

Meta-Analysis

Effective rate

The outcome indicators of the 8 RCTs included clinical effective rate. According to the different interventions in the experimental group, the studies were divided into two subgroups for analysis: Xuefu Zhuyu Oral Liquid alone and Xuefu Zhuyu Oral Liquid combined with conventional treatment. The heterogeneity testing showed good homogeneity between the groups of Xuefu Zhuyu Oral Liquid *vs*. conventional treatment (P= 0.72, I^2=0%), so a fixed-effect model was used for the analysis. The analysis result showed that the therapeutic effect of Xuefu Zhuyu Oral Liquid alone was better than that of conventional treatment (RR=1.22, 95%CI

Table 1. Basic Information Included in the Studies

No.	Author & Year	Sample size		Male/female		Age/years		Intervention		Course of treatment/d	Outcome index
		T	C	T	C	T	C	T	C		
1	Hu Xinping 2001[14]	30	30	18/42		23–60		Xuefu Zhuyu Oral Liquid	flunarizine hydrochloride capsule	14	total effective rate+hemorheology+TCD
2	Shi Lei 2005[15]	60	58	24/36	26/32	41.5	40.1	Xuefu Zhuyu Oral Liquid+CT	flunarizine hydrochloride capsule	14–20	total effective rate
3	Cong Chunyan 2005[16]	69	63	—		—		Xuefu Zhuyu Oral Liquid	rotundine+vitamin	30	total effective rate
4	Hu Yongtao 2006[17]	42	38	14/28	13/25	17–45	18–46	Xuefu Zhuyu Oral Liquid+ CT	tiapride+oryzanol	30	total effective rate
5	He Suqin 2008[18]	50	48	20/30	15/33	33.2	30.5	Xuefu Zhuyu Oral Liquid	flunarizine hydrochloride capsule	30	total effective rate
6	Liu Guofeng 2009[19]	30	30	9/21	10/20	18/42	19/40	Xuefu Zhuyu Oral Liquid+ CT	ingram tablet+ yuntongding tablet	14	total effective rate
7	Liu Aiping 2010[20]	60	58	18/42	19/39	42	39.6	Xuefu Zhuyu Oral Liquid+ CT	nimodipine tablet	14	total effective rate
8	Ma Weina 2013[21]	21	19	8/13	7/12	41.2	39.8	Xuefu Zhuyu Oral Liquid+ CT	flunarizine hydrochloride capsule	14	total effective rate

Note: T. Experimental group; C. Control group; CT. Conventional treatment; —. Unknown data.

(C)1994-2024 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net

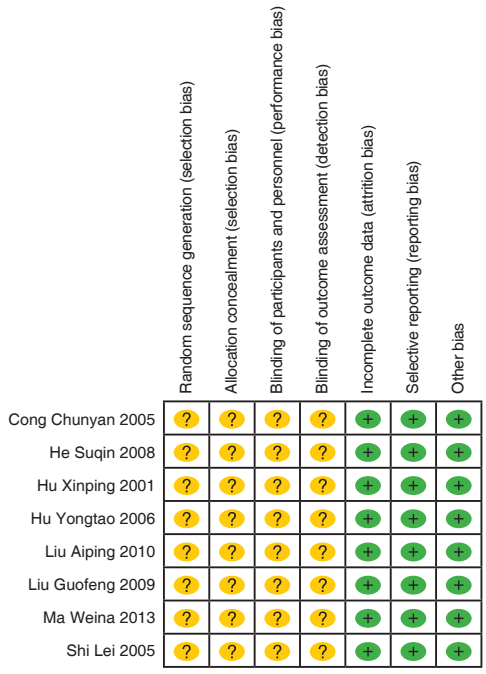


Figure 3. Summary of the Risk of Bias

[1.11, 1.33], *P*<0.0001), as shown in Figure 4. The homogeneity between subgroups of Xuefu Zhuyu Oral Liquid combined with conventional treatment was good (*P*=0.87, I^2=0%), and a fixed-effect model was also used for the analysis. The result showed that the therapeutic effect of Xuefu Zhuyu Oral Liquid combined with conventional treatment was better than that of conventional treatment alone (RR=1.19, 95%CI [1.11, 1.28], *P*<0.0001), and the difference was statistically significant, as shown in Figure 5.

Cure rate

The cure rate was analyzed in two subgroups: Xuefu Zhuyu Oral Liquid alone and Xuefu Zhuyu Oral Liquid combined with conventional treatment. The former included 2 studies,[14,18] and the latter included 5 studies.[15,17,19-21] The heterogeneity testing showed that the homogeneity among the groups treated with Xuefu Zhuyu Oral Liquid and conventional treatment was good (*P*=1.00, I^2=0%), so a fixed effect model was used for the analysis. The result showed no significant difference in cure rate between the two groups (*P*=0.17), as shown in Figure 6. The homogeneity between subgroups of Xuefu Zhuyu Oral Liquid combined with conventional treatment was moderate (*P*=0.04, I^2=59%), so a random-effect model was used for the analysis. The result showed that the cure rate was higher in the group treated with Xuefu Zhuyu Oral Liquid combined with conventional treatment than that of conventional treatment alone (RR=1.65, 95%CI [1.17, 2.34], *P*=0.005), and the difference was statistically significant, as shown in Figure 7.

Blood Rheology and TCD

In addition to the clinically effective rate and cure rate, Hu Xinping's[14] study also involved blood rheology and Transcranial Doppler Ultrasonography (TCD) as outcome indicators. The result showed that Xuefu Zhuyu Oral Liquid significantly improved blood rheology, which was superior to the control group (*P*>0.05). TCD examination showed a significant dilation of the cerebral arteries (MCA, BA and VA) after treatment (*P*>0.05), with no significant difference from the control group (*P*>0.05).

Adverse Reactions

Only 3 studies[15,17,19] reported that individual

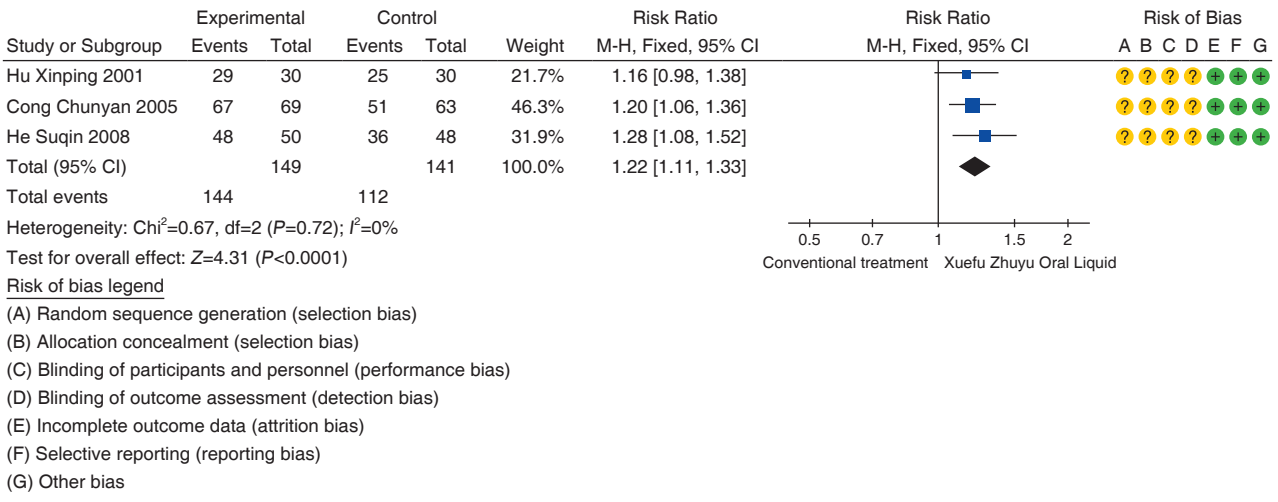
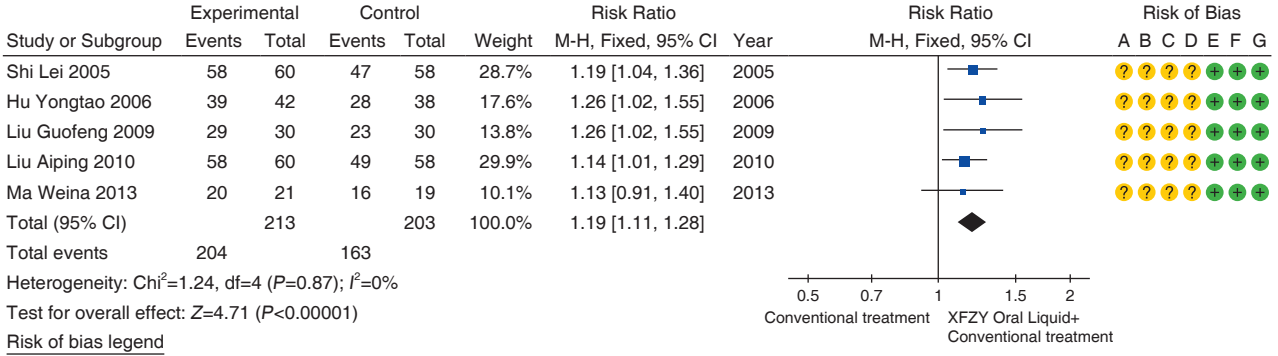


Figure 4. Forest Plot of the Clinical Efficiency of Conventional Treatment *VS* Xuefu Zhuyu Oral Liquid

(C)1994-2024 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net



Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

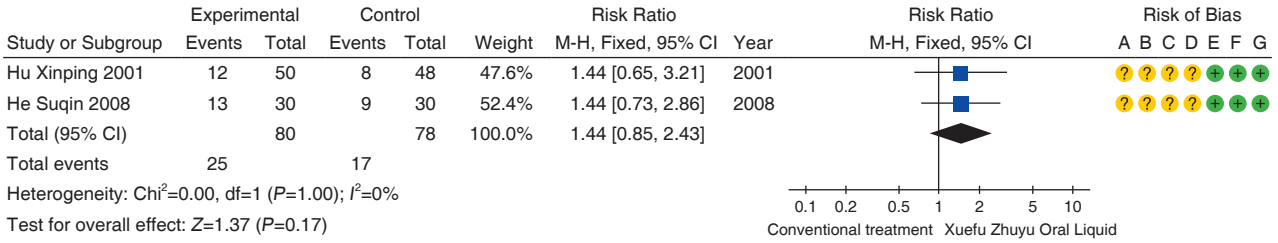
(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

Figure 5. Forest Plot of the Clinical Efficiency of Conventional Treatment *VS* Xuefu Zhuyu Oral Liquid+CT



Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

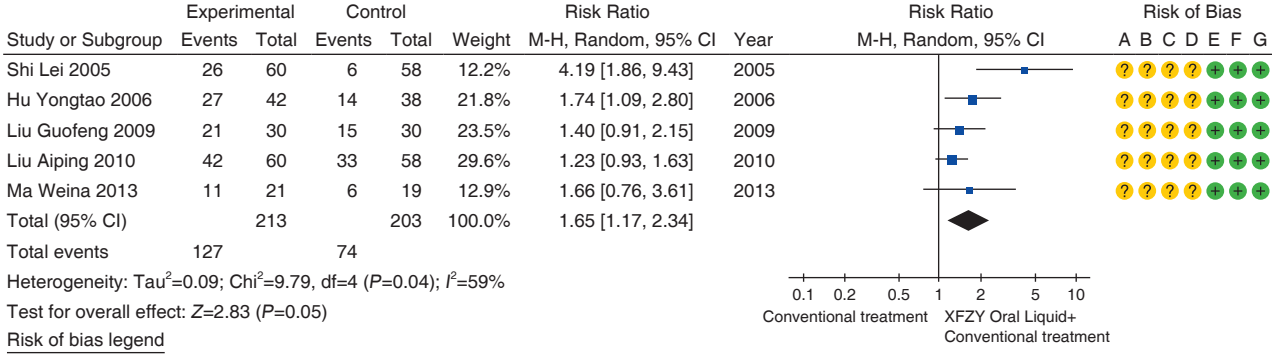
(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

Figure 6. Forest Plot of Cure Rate of Conventional Treatment *VS* Xuefu Zhuyu Oral Liquid



Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

Figure 7. Forest Plot of Cure Rate of Conventional Treatment *VS* Xuefu Zhuyu Oral Liquid+Conventional Treatment

(C)1994-2024 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net

patients experienced mild adverse reactions during treatment, such as transient diarrhea, nausea, lethargy, etc, and symptoms improved after symptomatic treatment. Among them, only the study by Liu Guofeng[19] reported that adverse reactions occurred only in the control group, with 1 case of dry mouth and nausea, and 1 case of lethargy. In contrast, the other 2 studies[15,17] did not report the group in which adverse reactions occurred, as shown in Table 2. The adverse reactions mentioned in the studies were not directly related to Xuefu Zhuyu Oral Liquid. Overall, it was evident that Xuefu Zhuyu Oral Liquid is a safe and effective drug for the treatment of migraine.

Table 2. Adverse Drug Reaction

Author & Year	Experimental group	Control group
Shi Lei 2005[15]	Individual patients experienced transient diarrhea and lethargy	
Hu Yongtao 2006[17]	A few patients had mild adverse reactions after taking the medication	
Liu Guofeng 2009[19]	—	Dry mouth and nausea *n*=1 Lethargy *n*=1

DISCUSSION

Efficacy of Xuefu Zhuyu Oral Liquid in the Treatment of Migraine

A total of 8 RCTs with 706 cases were included in this study, including 362 cases in the experimental group and 344 cases in the control group. The subgroup of Xuefu Zhuyu Oral Liquid *vs*. conventional treatment included 3 studies, and the subgroup of Xuefu Zhuyu Oral Liquid combined with conventional treatment vs. conventional treatment included 5 studies. The outcome indicators of 8 RCTs all included clinically effective rate, and all reported cure rate except Cong Xinyan's study. In addition, the outcome indicator of Hu Xinping's study also involved blood rheology and TCD. The meta-analysis results suggest that the clinical efficiency of Xuefu Zhuyu Oral Liquid alone or in combination with conventional treatment for treating migraine may be better than that of conventional treatment.

Migraine long-term attack can lead to neurological and psychological dysfunction. Currently, the main drugs available for the treatment of migraine are the triptans, NSAIDs and other western medicine treatments. While these medications can improve the symptoms of headaches, their long-term application is associated with significant adverse reactions. Additionally, discontinuing these medications can lead to recurring symptoms, making it difficult to meet the actual needs of patients. In recent years, more and more scholars have been attempting to seek breakthroughs with traditional Chinese medicine. In traditional Chinese medicine, migraines belong to the category of "head wind" or "first wind".[22] They are caused by external factors or internal imbalances that lead to blood vessel spasms, resulting in poor circulation of qi and blood, blood stasis blocking the head, and obstruction of the meridians in the head, resulting in pain. Migraines mainly manifest as "pain" with typical features such as pain occurring on one side of the head, a relatively long duration, and recurrent episodes. These characteristics align with the pathogenic feature of "blood stasis". The different patterns and development stages of headache often involve blood stasis symptoms.

Xuefu Zhuyu Oral Liquid is a modified dosage form of the classical Chinese medicine formula "Xuefu Zhuyu Decoction", with the same proportions of ingredients as the original formula. It primarily treats chest pain and long-standing headaches caused by qi stagnation and blood stasis. Xuefu Zhuyu Decoction, which originated from *Yilin Gaicuo* <<医林改错>> by Wang Qingren in the Qing Dynasty, is a representative formula for activating blood and removing blood stasis. It is based on Taohong Siwu Decoction (桃红四物汤), supplemented by Sini Powder (四逆散) to soothe the liver and regulate qi, Nuixi to promote the downward movement of blood, and Jiegeng to facilitate the upward movement of medicinal ingredients.[23] Within the formula, Honghua is the principal herb, activating blood circulation, dispersing blood stasis, and relieving pain. Chuanxiong, known for its ability to promote qi and blood circulation, dispel wind and remove blood stasis, is a crucial herb for treating headaches. Chaihu can soothe the liver and relieve stagnation. Zhiqiao and Jiegeng are used to ascend and descend, regulate the movement of qi. Gancao harmonizes the other herbs, easing urgency and pain. Moreover, a large number of blood-activating and stasis-resolving herbs are combined in the formula. The formula combines qi and blood herbs,

(C)1994-2024 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net

effectively regulating qi stagnation and eliminating blood stagnation. It simultaneously nourishes and promotes blood circulation, which promotes qi and relieves pain, activates blood and removes blood stasis, widely used in treating chest pain and headache caused by qi and blood coagulation.[24] Modern pharmacological research suggests that Xuefu Zhuyu Decoction and its related preparations can promote blood circulation and eliminate blood stasis through multiple pathways and targets, such as inhibiting platelet adhesion and aggregation, moderately regulating angiogenesis, and improving inflammatory levels, which can alleviate headache symptoms and reduce the frequency of headache attacks.[25-27] Taoren and Honghuahua can inhibit platelet aggregation and exhibit anti-inflammatory effects.[28] They can improve microcirculation in blood vessels, accelerate blood flow in cerebral arteries, and ameliorate cerebral tissue ischemia. Additionally, Niuxi can improve blood circulation in the head by preventing platelet aggregation, relaxing vascular smooth muscle, dilate blood vessels by relaxing vascular smooth muscle, and thereby alleviating pain.

Xuefu Zhuyu Oral Liquid is a liquid formulation made by extracting effective ingredients from the Xuefu Zhuyu Decoction. The manufacturing process and active substances are relatively transparent, ensuring stable drug quality and a high level of medication safety. Oral liquid is a commonly used traditional Chinese medicine dosage form. It is typically packaged in single doses, making it convenient for carrying and taking. Liquid formulations allow for faster and more thorough absorption after administration, ensuring that medications take effect quickly.

Safety of Xuefu Zhuyu Oral Liquid in the Treatment of Migraine

Among the 8 studies included in the analysis, a total of 3 studies reported adverse events, all of which were mild and not directly related to Xuefu Zhuyu Oral Liquid, indicating a relatively high safety in the treatment for migraine. According to the instruction of Xuefu Zhuyu Oral Liquid, adverse reactions such as nausea, vomiting, abdominal distension, abdominal pain, diarrhea, rash, pruritus, and flushing may occur. There have been allergic reactions reported, but no reports of severe adverse reactions have been observed, suggesting that Xuefu Zhuyu Oral Liquid has good safety for treating migraine.

Study Limitations

The evidence evaluated by this system suggests that to some extent, the single or combined use of Xuefu Zhuyu Oral Liquid has a positive impact on relieving migraines, and it is generally safe. However, different western conventional medications, such as flunarizine and nimodipine were uniformly classified as conventional treatment in this study, which may have heterogeneity due to the differences in specific medications among studies, thus impacting the study result. In this study, we searched and analyzed the published RCTs on the treatment of migraine with Xuefu Zhuyu Oral Liquid. However, most of the studies included in this analysis were conducted many years ago and had limited sample sizes, so the methodological quality of the literature was generally poor. The studies included in the analysis only mentioned the word "randomization", none of which reported the specific randomization method. Therefore, it was difficult to judge whether randomization was conducted, which affected the quality of the evidence for the efficacy of Xuefu Zhuyu Oral Liquid in treating migraines. Currently, the methodological quality of relevant researchs is poor. In the future, more high-quality original studies with large samples, scientific design, multi-center, and rigorous implementation should be conducted to explore the effectiveness and safety of Xuefu Zhuyu Oral Liquid in treating migraine, in order to improve the scientificity and credibility of the literature and provide high-quality evidence for the clinical application of Xuefu Zhuyu Oral Liquid. We recommend that clinical researchers proactively register their trial protocols, for example, in the Chinese Clinical Trial Registry. When reporting the results of RCTs involving herbal interventions, strict adherence to the CONSORT 2010 statement for the reporting of RCTs is necessary. This includes clearly specifying the randomization methods, detailing the implementation of allocation concealment and blinding, and comprehensively recording cases of attrition to strengthen quality control.

(C)1994-2024 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net

Clinical Guidance Significance

The results of meta-analysis showed that the combined application of Xuefu Zhuyu Oral Liquid in the treatment of migraine was more effective than conventional therapy. In addition, the efficacy of Xuefu Zhuyu Oral Liquid alone in the treatment of migraine was also better than conventional therapy, indicating that it can effectively relieve headache and its accompanying symptoms, reduce the recurrence of headache, and improve the quality of patients' survival, with no significant adverse effects and a relatively high safety. Therefore, Xuefu Zhuyu Oral Liquid can be applied alone if the migraine attack is mild, and can combine with the conventional treatment when the condition is severe. This study systematically searched and analyzed the published RCT studies on the treatment of migraine with Xuefu Zhuyu Oral Liquid. However, considering that most of the included original studies were conducted a long time ago and the methodological quality of the literature was generally low, may affect the quality of effective evidence for the conclusions of this study. Therefore, using the medication in clinical practice, physicians should take into account the specific clinical situation and refer to the findings of this study, and then combine clinical experience and patients' preference to determine the treatment plan.

CONCLUSION

In summary, the available literature and systematic evaluation demonstrate that the application of Xuefu Zhuyu Oral Liquid alone or in combination with conventional treatment can improve the efficiency of treating migraine without serious side effects. More large-sample, scientifically designed, multi-center, rigorously implemented, high-quality original studies are still needed in the future to further validate the efficacy and safety of Xuefu Zhuyu Oral Liquid in the treatment of migraine.

REFERENCES

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia, 2018, 38(1): 1-211.
2. Pelzer N, Louter MA, Van Zwet EW, et al. Linking migraine frequency with family history of migraine. Cephalalgia, 2019, 39(2): 229-236.
3. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet, 2017, 390(10100): 1211-1259.
4. Ashina M, Hansen JM, Do TP, et al. Migraine and the trigeminovascular system-40 years and counting. Lancet Neurol, 2019, 18(8): 795-804.
5. Zhou X, Sun ZW. The pathogenesis, diagnosis and treatment progress of migraine. Chinese Journal of General Practice, 2019, 17(5): 714-715.
6. Jiang XG. New progress in the pathogenesis and treatment of migraine. Journal of Neurology and Neurorehabilitation, 2019, 15(2): 80-88.
7. Lombard L, Farrar M, Ye W, et al. A global real-world assessment of the impact on health-related quality of life and work productivity of migraine in patients with insufficient versus good response to triptan medication. J Headache Pain, 2020, 21(1): 41.
8. Long QE, Zhao L, Zhang CL. A retrospective study of 972 cases of adverse reactions/events related to opioid drugs. Chinese Journal of Pharmacoepidemiology, 2019, 28(5): 314-318.
9. Wang JX, Kong XH, Guo DH, et al. Analysis of 5,597 adverse reaction reports of non-steroidal anti-inflammatory drugs. Chinese Journal of Pharmacoepidemiology, 2021, 30(7): 457-461.
10. Yang HT, Wang EL. Research progress in traditional Chinese medicine treatment of migraine based on staging and syndrome differentiation. Chinese Journal of Integrative Medicine on Cardio-Cerebrovascular Disease, 2022, 20(6): 1035-1040.
11. Guo Z, Wang H, Zhu XN, et al. Flunarizine combined with Xuefu Zhuyu Decoction treating 36 cases of migraine. Western Journal of Traditional Chinese Medicine, 2019, 32(6): 102-104.
12. Mao LT, Huang NP, Xiang JJ, et al. Overview of CM Treatment of Migraine with Blood Stasis Syndrome. Asia-Pacific Traditional Medicine, 2023, 19(12): 235-239.
13. Head and facial pain group, Pain Society of Chinese Medical Association. Guidelines for the prevention and treatment of migraine in China. Chinese Journal of Pain Medicine, 2016, 22(10): 721-727.
14. Hu XP. Clinical observation of 30 cases of migraine treated with Xuefu Zhuyu Oral Liquid. Jilin Journal of Chinese Medicine, 2001, 6: 22.
15. Shi L, Wang F. Observation of therapeutic effects of 60

(C)1994-2024 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net

cases of migraine treated with a combination of flunarizine hydrochloride and Xuefu Zhuyu Oral Liquid. The Journal of Medical Theory and Practice, 2005, 11: 45-46.

16. Cong CY, Ren LJ, Cong G. Observation of therapeutic effects of Xuefu Zhuyu Oral Liquid on 69 cases of migraine. Compilation of papers at the 6th national academic conference on the study of blood stasis syndrome and promoting blood circulation and resolving stasis in combination of traditional Chinese and western medicine, 2005: 266.
17. Hu YT, Zhang J, Yu CY, et al. The treatment of migraine with Xuefu Zhuyu Oral Liquid and tiapride. Modern Journal of Integrated Traditional Chinese and Western Medicine, 2006, 17: 2346, 2352.
18. He SQ. Clinical Observation on the treatment of migraine with Xuefu Zhuyu Oral Liquid. Journal of Liaoning University of Traditional Chinese Medicine, 2008, 8: 109-110.
19. Liu GF, Guo SY. Clinical experience of treating 30 cases of migraine with integrated traditional Chinese and western medicine. China Medical Herald, 2009, 6(32): 55-56.
20. Liu AP. Treatment of 60 cases of migraine with a combination therapy of Xuefu Zhuyu Oral Liquid and nimodipine tablets. Inner Mongolia Journal of Traditional Chinese Medicine, 2010, 29(8): 24.
21. Ma WN. Observation of clinical efficacy of a combination therapy of Xuefu Zhuyu Oral Liquid and flunarizine hydrochloride in treating migraine. Chinese Journal of General Practice, 2013, 11(1): 100.
22. Zhao DM, Cheng HL. Clinical efficacy and influence on hemodynamics of Xuesaitong in treating elderly patients with migraine. Shaanxi Journal of Traditional Chinese Medicine, 2016, 37(4): 430-431.
23. Fan XW, Li X, Li BL. Clinical experience in the application of Xuefu Zhuyu Decoction. China Practical Medicine, 2020, 15(28): 204-206.
24. Li JF, Dong H, Cao JM. Clinical experience of chief physician Dong Hong in treating migraine. Asia-Pacific Traditional Medicine, 2017, 13(22): 91-92.
25. He X, Duan X, Liu J, et al. The antiinflammatory effects of Xuefu Zhuyu Decoction on C3H/HeJ mice with alopecia areata. Phytomedicine, 2021, 81: 153423.
26. Shi WL, Lu PF, Gao D, et al. Effect of Xuefu Zhuyu Capsule on Angiogenesis in Hindlimb Ischemic Rats. Chinese Journal of Integrative Medicine, 2020, 26(1): 39-45.
27. Hu YQ, Zhang JS, Lin F, et al. Experimental study on the regulation of EphB4/EphrinB2 to promote moderate blood vessel growth by Xuefu Zhuyu Capsules. Chinese Journal of Integrated Traditional and Western Medicine, 2017, 37(2): 209-214.
28. Pan L, Peng C, Wang L, et al. Network pharmacology and experimental validation-based approach to understand the effect and mechanism of Taohong Siwu Decoction against ischemic stroke. Journal of Ethnopharmacology, 2022, 294: 115339.

(Received August 19, 2023)

(C)1994-2024 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net