SYSTEMATIC REVIEW

Analysis of clinical efficacy of Si Miao decoction combine with acupuncture and cupping treatment for gout: a systematic review and meta-analysis [version 1; peer review: 2 approved with reservations]

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Abstract

This systematic review has been aimed to evaluate the clinical efficacy of the Si Miao decoction combined with acupuncture and cupping treatment for Gout. Three English and Chinese databases were searched for articles related to the effect of the Si Miao decoction combine with acupuncture and cupping therapy on CRP, UA, and ESR in Gout. The time period was limited from 01 January 2010 till 31 August 2019. Meta-analysis was performed using both the random and fixed effects model, and I^2 was used to evaluate the heterogeneity. Identification was made through database searching of 238 publications. Three articles were eligible. Following the Si Miao Decoction combined with acupuncture and cupping therapy there was a significant reduction in the clinical parameters (SMD: -0.91 , 95% CI: -1.081 , -0.741 , $p = 0.000$) (OR: -1.652 , 95% CI: -1.960 , -1.344 , $p = 0.000$). High heterogeneity tests were indicated ($Q=146.548$, $P = 0.00$, $I^2 = 94.54\%$). This systematic review and meta-analysis indicated that the Si Miao decoction combined with acupuncture and cupping therapy significantly reduced the circulating levels of UA, ESR, and CRP. There is a need to improve the methodologies of clinical trials on modified Si Miao decoction combined with Acupuncture and Cupping treatment.

Keywords

Si Miao, Decoction, Acupuncture, Cupping

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Abbreviations

Std= Standard; **CRP**= C-reactive protein; **ESR**= Erythrocyte sedimentation rate; **SDM**= standard difference in mean; **Hg**= hedge's g; **OR**= odds ratio; **SPDM**= Standard paired difference; **CORR**= Correlation; **CONSORT**= Consolidated Standards of Reporting Trials; **OSF**= Center for Open Science; **M-Si-M**= Modified Si Miao; **WM**= Western medicine; **WHO**= World Health organization; **M-Si-M+Ac+Cu**= **Ac**=Si Miao Decoction combine with acupuncture and cupping therapy; **Ac**=Acupuncture; **Cu**= Cupping.

Introduction

Arthritis is defined as the swelling of a joint that is accompanied by a limitation of motion, and increase in heat, pain, or tenderness¹. Gout is a systemic disease which is also known as podagra and is caused by the presence of crystals of monosodium urate inside the tissues. These crystals trigger the inflammatory response that results in painful swelling mainly over the big toe². Gouty arthritis can cause significant disability amongst patients that results in the dysfunction of normal self-care and recreational, social, and work activities³.

Gout is considered as one of the most prevalent inflammatory diseases. The general prevalence of gout is 1–4% of the general population⁴. It is affects people in different parts of the world including the UK (2.5% of the total population)⁵, Korea (1.94% per 1000 persons)⁶, and New-Zealand (2.69% Aotearoa New Zealand Health Tracker population)⁷.

Description of the intervention

Si Miao is the herbal combination of *Cortex Phellodendri Chinensis*, *Rhizoma Atractylodis Lanceae*, *Radix Achyranthis Bidentatae*, and *Semen Coicis Lachryma-Jobi*. It is also well known as the Four-Marvels Pill⁸. It is also available in a modified form with some additional herbs in actual formulation and has been used in the treatment of gout and arthritis. Acupuncture has been used to treat health conditions, including pain, for over 3,000 years, yet it has only been in the last half a century that biochemistry and neural imaging advances have allowed for the scientific understanding of its physiological mechanisms⁹. A number of studies have found the effectiveness of acupuncture in the treatment of gouty arthritis^{10,11}. Lee, *et al.* have performed a systematic review on acupuncture for gouty arthritis and found it to be an effective complementary medicine¹². Cupping therapy, commonly known as Al-hijamah in Islamic medicine, is also well-known amongst traditional practitioners in treating arthritis^{12–14}.

How the intervention might work

Modified Si Miao San extract inhibits an inflammatory response and modulates insulin sensitivity in hepatocytes through an IKK β /IRS-1/Akt-dependent pathway¹⁵. Acupuncture helps in reducing the pain and inflammation through an increase in IL-10 concentrations in the muscle¹⁶. Wet cupping helps to remove oxidants and reduce the oxidative stress through oxidative balance¹⁷. The imbalance of oxidative stress will result in an increase in the inflammatory response¹⁸.

Methods

A systematic literature search strategy was prepared according to the given guidelines by Cochrane infectious diseases¹⁹. Si Miao, Si Miao San, Si Miao Pian, Si Miao Wan, Gout and arthritis were the main keywords used during the search from different databases, such as PubMed, PubMed Central, and CNKI with the publication range being from 01 January 2010 till 31 August 2019. The literature works identified had been searched for in the English and Chinese languages. The list of keywords used in the English and Chinese versions have been mentioned in Table 1. The initial search syntax for PubMed and PubMed Central consisted of the following list.

1. (Si[All Fields] AND Miao[All Fields]) AND (“gout”[MeSH Terms] OR “gout”[All Fields]) AND (“2010/01/01”[PDAT] : “2019/08/31”[PDAT]); Si Miao[Text Word] AND Gout[Text Word] AND (“2010/01/01”[PubDate] : “2019/08/31”[PubDate])
2. (Si[All Fields] AND Miao[All Fields]) AND (“arthritis”[MeSH Terms] OR “arthritis”[All Fields]) AND (“2010/01/01”[PubDate] : “2019/08/31”[PubDate]); Si Miao[Text Word] AND arthritis[Text Word] AND (“2010/01/01”[PubDate] : “2019/08/31”[PubDate])
3. (Si[All Fields] AND Miao[All Fields] AND San[All Fields]) AND (“gout”[MeSH Terms] OR “gout”[All Fields]) AND (“2010/01/01”[PDAT] : “2019/08/31”[PDAT]); Si Miao San[Text Word] AND Gout[Text Word] AND (“2010/01/01”[PubDate] : “2019/08/31”[PubDate])
4. (Si[All Fields] AND Miao[All Fields] AND San[All Fields]) AND (“arthritis”[MeSH Terms] OR “arthritis”[All Fields]) AND (“2010/01/01”[PDAT] : “2019/08/31”[PDAT]); Si Miao San[Text Word] AND arthritis[Text Word] AND (“2010/01/01”[PubDate] : “2019/08/31”[PubDate])
5. (Si[All Fields] AND Miao[All Fields] AND Pian[All Fields]) AND (“gout”[MeSH Terms] OR “gout”[All Fields]) AND (“2010/01/01”[PDAT] : “2019/08/31”[PDAT]); (Si Miao Pian[Text Word]) AND gout[Text Word] AND (“2010/01/01”[PubDate] : “2019/08/31”[PubDate])
6. (Si[All Fields] AND Miao[All Fields] AND Pian[All Fields]) AND (“arthritis”[MeSH Terms] OR “arthritis”[All Fields])

Table 1. List of keywords used for the identification of literature.

Database	Keywords
PubMed, PubMed Central	Si Miao, Si Miao San, Si Miao Pian, Si Miao Wan, Gout, arthritis
CNKI	加味四妙散(Jia Wei Si Miao San), 四妙散 (Si Miao San), 丸 (Capsule), 片 (Pill), 汤 (Decoction), 痛风 (Tòngfēng) (Gout)

AND ("2010/01/01"[PDAT] : "2019/08/31"[PDAT]); (Si Miao Pian[Text Word]) AND arthritis[Text Word] AND (("2010/01/01"[PubDate] : "2019/08/31"[PubDate]))

7. (Si[All Fields] AND Miao[All Fields] AND Wan[All Fields]) AND gout[All Fields] AND ("2010/01/01"[PDAT] : "2019/08/31"[PDAT])
8. (Si[All Fields] AND Miao[All Fields] AND Wan[All Fields]) AND arthritis[All Fields] AND ("2010/01/01"[PDAT] : "2019/08/31"[PDAT])

Literature screening

A total number of 238 (n=238) articles were identified from different databases (PubMed, PubMed Central, and CNKI). The records were screened in two stages on the basis of number of duplications followed by some initial criteria where irrelevant articles, review articles, and animal and chemical studies had been excluded. After the initial screening, 132 (n=132) articles were identified. Microsoft Excel 2016²⁰ and Mendeley version 1.19.2²¹ were used for data deduplication and citation management.

Eligibility criteria

The included studies were based upon the use of the modified Si Miao (M-Si-M) combined with acupuncture and cupping for the treatment of gout and arthritis. The selected studies included both the Chinese and English languages but most of the studies available were in the Chinese language. The articles that focussed on the Si Miao formulation, modified Si Miao (M-Si-M) or combination of modified Si Miao (M-Si-M) with western medicine were excluded. After the application of the eligibility criteria, the number of articles had been reduced to six (n=6) articles and 126 articles (n=126) had been excluded. One article (n=1) had been removed further for qualitative synthesis and data extraction because of the absence of a randomised clinical trial (RCT). Clinical effectiveness, uric acid (UA), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were accessed as the main outcome whereas the visual analogue Scale (VAS) and symptom scale had been excluded. Two articles (n=2) had been excluded because of unavailable outcome indicators which restrict the use to only three studies (n=3) for the meta-analysis. The flow chart of the study's selection process according to the PRISMA flow diagram has been mentioned in [Figure 1](#).

Figure 1. Flow chart of study selection process. PRISMA flow chart of the selection process of Si Miao decoction combine with acupuncture and cupping therapy.

Data extraction

The Cochrane Handbook for Systematic Reviews of Interventions²² and JBI Systematic Reviews were used as reporting channels to assess the quality of the manuscript²³. Two researchers independently evaluated the quality of the included studies, and a third party was consulted for resolution of any disagreement. The study design, participants, intervention, and outcome (SPIO) criteria have been mentioned in Table 2. The authors evaluated the methodological assessment under: aim/hypothesis clearly defined, adequate sample representation, patient care quality assurance, ethical approval protocol number, outcome clearly described, validity and reliability of

outcome measure, attempt to blind researcher, follow-up, appropriate statistical analysis, and missing data reported (Figure 2). The bias assessment of the studies included in the qualitative synthesis included random sequence, allocation concealment, selective reporting, blinding of participants and personnel, blinding of outcome assessment, and incomplete outcome data according to the Cochrane guidelines (Table 3)²². The study characteristics of the selected studies were assessed according to the study design, treatment, control, statistical tool used, software to assess the outcome, and final outcome of the findings (Table 4). Uric acid, erythrocyte sedimentation rate, and C-reactive protein were the clinical parameters used after the

Table 2. Study design; participants; intervention; outcome (SPIO) criteria.

	Inclusion Criteria	Exclusion Criteria
Study design	Randomized, clinical trial, full-length, Si Miao decoction combine with acupuncture and cupping therapy	All review articles, irrelevant articles, duplicate, chemical studies, in vivo studies, Si Miao formulation, Modified Si Miao (M-Si-M) or western combination
Participants	Between 23 to 70 years	Below 23 years or above 70 years of age were excluded.
Intervention	<i>Si Miao</i> combination with acupuncture and cupping were indicated in the treatment of gout and arthritis.	-
Outcomes	Clinical effectiveness, uric acid (UA), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)	Visual Analogue Scale (VAS), Symptom scale (SS)

Figure 2. Methodological assessment of the five studies included for qualitative synthesis (0=No/not reported, 1=Yes).

Table 3. Bias assessment of the studies included in qualitative synthesis according to the Cochrane guidelines.

Study and year	Random sequence generation	Allocation concealment	Selective reporting	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data
Zhang, <i>et al.</i> , 2019 ²⁴						
Jia, <i>et al.</i> , 2016 ²⁵						
Chen, <i>et al.</i> , 2015 ²⁶						
Deng, <i>et al.</i> , 2017 ²⁷						
Yu, <i>et al.</i> , 2013 ²⁸

Low
 High
 Unclear

Table 4. Study characteristics for Qualitative synthesis.

Author, year	Study Design	Observed/ Treatment	Control	Statistical analysis	Software	Outcomes
Zhang, <i>et al.</i> , 2019 ²⁴	Randomized clinical trial	Acupuncture combined with modified Si Miao Powder	Western Medication	Chi-squared test	SPSS21.0	VAS, Clinical effectiveness, CRP, ESR, UA
Jia, <i>et al.</i> , 2016 ²⁵	Randomized clinical trial	Blood-letting combined with modified Si Miao Decoction	Western Medication	Chi-squared test	SPSS16.0	VAS, Clinical effectiveness, WBC, ESR, CRP, UA
Chen, <i>et al.</i> , 2015 ²⁶	Randomized clinical trial	Blood-letting combined with modified Si Miao Powder	Western Medication	t-test	SPSS17.0	VAS, UA
Deng, <i>et al.</i> , 2017 ²⁷	Randomized clinical trial	Blood-letting combined with Si Miao Powder	Western Medication	t-test	SPSS20.0	VAS, Clinical effectiveness, UA, CRP, ESR
Yu, <i>et al.</i> , 2013 ²⁸	Randomized clinical trial	Auricular Acupressure combined with Si Miao Powder	Western Medication	t-test	SPSS13.0	VAS, Clinical Symptoms, UA

treatment and further evaluation for the meta-analysis (Table 5). Microsoft Excel 2016²⁰ (Microsoft Corporation, Redmond, WA) was used to extract the data, removing study duplications, and Mendeley desktop 1.19.2²¹ was used for importing the references.

Quantitative data synthesis

Comprehensive Meta-Analysis (CMA) V2 software (Biostat, NJ) was used for data synthesis. Heterogeneity was quantitatively assessed using the I^2 index. An I^2 greater than 50% indicated significant heterogeneity amongst the studies. The results were expressed as mixed methods using both random and fixed effects. Effect sizes were expressed as odds ratio (OR), standard mean difference (SMD), Hedge's g (HG), Standard paired difference (SPD), Correlation (C), and 95% confidence interval (CI). A Z score was calculated to determine the overall effect. Funnel plot analysis was used to evaluate the presence of publication bias. The extent of variation amongst the effects

observed in different studies (between-study variance) is referred to as tau-squared, τ^2 , or Tau2²⁹.

Statistical analysis

Meta-analysis was conducted using the trial version of Comprehensive Meta-analysis (CMA) version 2.0 software³⁰. A forest plot displaying the standard difference in mean, Hedge's g , odds ratio, Standard paired difference, and Correlation 95% CIs for the impact of the observed therapy versus the control on different parameters were observed. True heterogeneity amongst the trials was assessed using the tau, T^{231} , and the extent of the inconsistency was measured by the I^2 index³².

Results

Clinical effect

All the included studies employed clinical effect as the outcome assessment. The clinical parameters included CRP, ESR, and

Table 5. Statistical characteristics of randomized trials of studies included for meta-analysis in treatment of gout and arthritis.

Variable in Treatment (T)	Zhang, <i>et al.</i> , 2019 (T)	Jia, <i>et al.</i> , 2016 (T)	Chen, <i>et al.</i> , 2015 (T)	Zhang, <i>et al.</i> , 2019 (C)	Jia, <i>et al.</i> , 2016 (C)	Chen, <i>et al.</i> , 2015 (C)	Variable in Control (C)
Sample size (N)	40	30	40	40	30	40	Sample size (N)
Age in years	43.28±9.34	41.78±6.62	41.85±7.12	44.37±8.26	43.66±6.00	41.85±7.12	Age in years
Uric acid (μmol/L) Before treatment	521.81±40.93	510.22±45.35	478.91±83.23	526.73±41.02	519.35±54.22	454.28±69.43	Uric acid (μmol/L) Before treatment
Uric acid (μmol/L) After treatment	376.03±27.21	367.32±31.71	398.06±79.82	442.91±30.28	401.85±47.28	413.65±84.57	Uric acid (μmol/L) After treatment
ESR (mm/h) Before treatment	44.23±9.07	58.56±32.31	53.26±24.76	45.11±9.10	55.32±31.33	50.94±22.52	ESR (mm/h) Before treatment
ESR (mm/h) After treatment	14.27±3.53	17.22±9.87	22.68±14.38	20.91±5.37	28.24±16.56	26.47±11.83	ESR (mm/h) After treatment
CRP (mg/L) Before treatment	60.91±6.38	44.25±29.33	10.61±4.03	61.64±6.11	46.65±31.66	11.32±4.25	CRP (mg/L) Before treatment
CRP (mg/L) After treatment	23.65±3.02	7.88±6.54	6.12±2.08	39.42±4.87	19.57±7.86	5.37±1.89	CRP (mg/L) After treatment
Significant Clinical effectiveness after treatment (N)	13	14	18	10	10	19	Significant Clinical effectiveness (N)
Insignificant Clinical effectiveness after treatment (N)	0	1	2	3	5	1	Insignificant Clinical effectiveness (N)

Data expressed Mean±SD

uric acid concentration after treatment with the modified Si Miao decoction combined with acupuncture and cupping therapy. The cumulative effect was observed by the meta-analysis of three randomised clinical treatment arms that suggested a significant reduction in the clinical parameters using the modified Si Miao decoction combined with acupuncture and cupping therapy (SMD: -0.91, 95% CI: -1.081, -0.741, $p = 0.000$) (OR: -1.652, 95% CI: -1.960, -1.344, $p = 0.000$). The forest plot, funnel plot of Cumulative std difference in means, and Log odds ratio of the Si Miao decoction combined with acupuncture and cupping therapy versus the Control have been expressed in the *Extended data* (Figures 3 and Figure 4), respectively. A high heterogeneity test was indicated ($Q=146.548$, $P = 0.00$, $I^2 = 94.54\%$) (*Extended data*: Figure 5). The estimated between-study variances of the cumulative Log odds ratio of the Si Miao decoction combined with acupuncture and cupping therapy versus the Control were $\tau=1.974$, $\text{Tau-squared} = 3.897$ with a standard error= 2.129, and variance= 4.533 (*Extended data*: Figure 5). The estimated between-study variances of the cumulative standard difference in means of the Si Miao decoction combined with acupuncture and cupping

therapy versus the Control were $\tau=1.088$, $\text{Tau-squared} = 1.184$ with a standard error= 0.647, and variance= 0.419 (*Extended data*: Figure 6).

Uric acid (UA)

Three studies measured blood uric acid as the outcome; a comparison between the observed versus the Control post-treatment was calculated. Data extracted from the three individual studies showed that heterogeneity existed ($Q=34.154$, $P = 0.000$, $I^2 = 94.144\%$) (*Extended data*: Figure 7). The fixed and random effects model was utilised for the statistical analysis. The estimated between-study variances of the std difference in the mean of the Si Miao decoction combined with acupuncture and cupping therapy versus the Control were $\tau=1.042$, $\text{Tau-squared} = 1.085$ with a standard error= 1.163, and variance= 1.353 (*Extended data*: Figure 7). The data suggested that the Si Miao decoction combined with acupuncture and cupping therapy could further decrease uric acid as compared to the control (SDM -0.960; 95% CI -1.240, -0.660; $P < 0.000$) (Hg -0.940; 95% CI -1.227, -0.652; $P < 0.000$) (OR 0.179; 95% CI 0.105, 0.302; $P < 0.000$) (SPDM -0.950; 95%

CI -1.240, -0.660; $P < 0.000$) (CORR -0.513; 95% CI -0.597, -0.417; $P < 0.000$) (*Extended data*: Figure 8). The funnel plot displaying the (A) standard difference in mean, (B) Hedge's g, (C) odds ratio, (D) Standard paired difference, and (E) Correlation 95% CIs for the impact of the observed therapy versus the Control on the uric acid concentrations have been represented in *Extended data* (Figure 9).

C-reactive protein (CRP)

Three studies measured blood Erythrocyte Sedimentation Rate (ESR) as the outcome; a comparison between the observed versus the Control post-treatment was calculated. The data extracted from the three individual studies showed that heterogeneity existed ($Q=12.092$, $P = 0.002$, $I^2 = 83.460\%$; *Extended data*: Figure 7). Fixed and random effects models were utilised for the statistical analysis. The estimated between-study variances of the std difference in the mean of the Si Miao decoction combined with acupuncture and cupping therapy versus the Control were $\tau = 0.556$, $\tau^2 = 0.310$ with a standard error = 0.372, and variance = 0.139 (*Extended data*: Figure 7). The data suggested that the Si Miao decoction combined with acupuncture and cupping therapy could further decrease the ESR as compared to the Control (SDM -0.808; 95% CI -1.087, 0.530; $P < 0.000$) (Hg -0.800; 95% CI -1.076, -0.524; $P < 0.000$) (OR 0.231; 95% CI 0.139, 0.383; $P < 0.000$) (SPDM -0.808; 95% CI -1.087, 0.530; $P < 0.000$) (CORR -0.400; 95% CI -0.500, -0.289; $P < 0.000$) (*Extended data*: Figure 10). The funnel plot displaying the (A) standard difference in mean, (B) Hedge's g, (C) odds ratio, (D) Standard paired difference, and (E) Correlation 95% CIs for the impact of the observed therapy versus the Control on the uric acid concentrations have been represented in the *Extended data* (Figure 11).

Three studies measured blood C-Reactive Protein (CRP) as the outcome; a comparison between the observed versus the Control post-treatment was calculated. The data extracted from the three individual studies showed that heterogeneity existed ($Q=99.391$, $P = 0.000$, $I^2 = 97.988\%$; *Extended data*: Figure 7). Fixed and random effects models were utilised for the statistical analysis. The estimated between-study variances of the std difference in the mean of the Si Miao decoction combined with acupuncture and cupping therapy versus the Control were $\tau = 2.056$, $\tau^2 = 4.228$ with a standard error = 4.483, and variance = 20.099 (*Extended data*: Figure 7). The data suggested that the Si Miao decoction combined with acupuncture and cupping therapy could further decrease the CRP as compared to the Control (SDM -3.892; 95% CI -4.637, -3.146; $P < 0.000$) (Hg -0.940; 95% CI -1.227, -0.652; $P < 0.000$) (OR 0.179; 95% CI 0.105, 0.302; $P < 0.000$) (SPDM -0.950; 95% CI -1.240, -0.660; $P < 0.000$) (CORR -0.513; 95% CI -0.597, -0.417; $P < 0.000$) (*Extended data*: Figure 12). The funnel plot displaying the (A) standard difference in mean, (B) Hedge's g, (C) odds ratio, (D) Standard paired difference, and (E) Correlation 95% CIs for the impact of the observed

therapy versus the Control on the uric acid concentrations have been represented in *Extended data* (Figure 13).

Discussion

Five studies were included for methodological assessment and inconsistencies were found in the methodology. Yu, *et al.* (2013)²⁸ was the only study in compliance with the key indicators for the methodological assessment followed by Deng, *et al.* (2017)²⁷. The Cochrane bias assessment also validated the results produced from the methodological assessment with most of the indicators being unclear and reporting of high risk of bias in random sequencing generation and blinding of the outcome assessment in Deng, *et al.* (2017)²⁷. Three ($n=3$) studies were considered for meta-analysis because the other two ($n=2$) studies were unable to comply with the eligibility criteria. This research has focused on comparing the randomised clinical trial of studies consisting of the combination of the Modified Si Miao (M-Si-M) with acupuncture (Ac) and cupping (Cu) treatment (M-Si-M+Ac+Cu) against that of western medicine. The clinical parameters of uric acid (UA)³³, Erythrocyte sedimentation rate (ESR), and C-Reactive protein (CRP) are important indicators in the treatment of arthritis and gout³⁴. The combination of the Modified Si Miao (M-Si-M) with acupuncture (Ac) and cupping (Cu) treatment was found to be better as compared with the western medicine (WM) but high heterogeneity was observed amongst all of the clinical parameters. High heterogeneity was observed because of methodological issues, such as problems with randomisation, early termination of trials, use of absolute rather than relative measures of risk, and publication bias³⁵. An improvement in the symptoms was observed when compared between the two treatments without any adverse effects.

This review is the first systematic review comparing the modified Si Miao decoction combined with acupuncture and cupping therapy (M-Si-M+Ac+Cu) against western medicine. There were a few limitations of this study, such as small sample size, lack of available research, and that most of the articles were published in China. Language was another barrier to report in this research as most the articles had been published in the Chinese language. There was also a high uncertainty in the methodology that led to publication bias. This evidence had been supported and verified in another systematic review on cupping therapy versus acupuncture for pain-related conditions³⁶. Further research on the same formulation is recommended with an improved clinical protocol using Consolidated Standards of Reporting Trials (CONSORT)³⁷. It is also recommended to register the protocol with ClinicalTrials.gov³⁸, Trial Registration by WHO³⁹ or ISRCTN registry⁴⁰. To increase the transparency and openness in the research, Science Europe⁴⁰ launched plan S⁴⁰ on 4 September 2018 that acknowledged the implementation of open archives and repositories to all journals. Therefore, it is recommended to increase the openness, integrity, and reproducibility of scientific research using the Centre for Open Science (OSF)⁴¹.

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

Extended data

Open Science Framework: Analysis of Clinical efficacy of Si Miao decoction combine with Acupuncture and Cupping treatment for Gout: A systematic review and meta-analysis, <https://doi.org/10.17605/OSF.IO/PUCX642>.

This project contains the following extended data:

- Figure 3: (A) Forest plot of Si Miao decoction combine with acupuncture and cupping therapy versus Control: cumulative std difference in means (B) Funnel plot of Si Miao decoction combine with acupuncture and cupping therapy versus Control: cumulative std difference in means
- Figure 4: (A) Forest plot of Si Miao Decoction combine with acupuncture and cupping therapy versus Control: Log odds ratio (B) Funnel plot of Si Miao Decoction combine with acupuncture and cupping therapy versus Control: Log odds ratio
- Figure 5: Heterogeneity and tau squared cumulative Log odds ratio of Si Miao Decoction combine with acupuncture and cupping therapy versus Control
- Figure 6: Heterogeneity and tau squared cumulative std difference in means of Si Miao Decoction combine with acupuncture and cupping therapy versus Control
- Figure 7: Heterogeneity and tau squared std difference in means of Si Miao Decoction combine with acupuncture and cupping therapy versus Control on outcomes parameters (A) ESR (B) CRP (C) Uric Acid
- Figure 8: Forest plot displaying (A) standard difference in mean for the impact of observed therapy versus control on uric acid concentrations. (B) Hedge's g for the impact of observed therapy versus control on uric acid concentrations. (C) Odds ratio for the impact of observed therapy versus control on uric acid concentrations. (D) Standard paired difference for the impact of observed therapy versus control on uric acid concentrations. (E) Correlation 95 % CIs for the impact of observed therapy versus control on uric acid concentrations.
- Figure 9: Funnel plot displaying (A) Standard difference in mean for the impact of observed therapy versus control on uric acid concentrations. (B) Hedge's g for the impact of observed therapy versus control on uric acid concentrations. (C) Odds ratio for the impact of observed therapy versus control on uric acid concentrations. (D) Standard paired difference for the impact of observed therapy versus control on uric acid concentrations. (E) Correlation 95 % CIs for the impact of observed therapy versus control on uric acid concentrations.

- Figure 10: Forest plot displaying (A) Standard difference in mean for the impact of observed therapy versus control on ESR concentrations. (B) Hedges' g for the impact of observed therapy versus control on ESR concentrations. (C) Odds ratio for the impact of observed therapy versus control on ESR concentrations. (D) Standard paired difference for the impact of observed therapy versus control on ESR concentrations. (E) Correlation 95 % CIs for the impact of observed therapy versus control on ESR concentrations.
- Figure 11: Funnel plot displaying (A) Standard difference in mean for the impact of observed therapy versus control on ESR concentrations. (B) Hedge's g for the impact of observed therapy versus control on ESR concentrations. (C) Odds ratio for the impact of observed therapy versus control on ESR concentrations. (D) Standard paired difference for the impact of observed therapy versus control on ESR concentrations. (E) Correlation 95 % CIs for the impact of observed therapy versus control on ESR concentrations.
- Figure 12: Forest plot displaying (A) Standard difference in mean for the impact of observed therapy versus control on CRP concentrations. (B) Hedge's g for the impact of observed therapy versus control on CRP concentrations. (C) Odds ratio for the impact of observed therapy versus control on CRP concentrations. (D) Standard paired difference for the impact of observed therapy versus control on CRP concentrations. (E) Correlation 95 % CIs for the impact of observed therapy versus control on CRP concentrations.
- Figure 13: Funnel plot displaying (A) Standard difference in mean for the impact of observed therapy versus control on CRP concentrations. (B) Hedge's g for the impact of observed therapy versus control on CRP concentrations. (C) Odds ratio for the impact of observed therapy versus control on CRP concentrations. (D) Standard paired difference for the impact of observed therapy versus control on CRP concentrations. (E) Correlation 95 % CIs for the impact of observed therapy versus control on CRP concentrations.

Reporting guidelines

Open Science Framework: PRISMA checklist for 'Analysis of clinical efficacy of Si Miao decoction combine with acupuncture and cupping treatment for gout: a systematic review and meta-analysis', <https://doi.org/10.17605/OSF.IO/PUCX642>.

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Yen-Ying Kung

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The authors used meta-analysis to evaluate the efficacy of Si Miao decoction combined with acupuncture and cupping treatment for gout in this manuscript. It is interesting but it still has some issues to be addressed as follows:

1. From the result, Si Miao decoction combined with acupuncture and cupping therapy reduced the levels of UA, ESR and CRP in patients with gout. However, it is hard to distinguish whether the efficiency in treating gout is only due to Si Miao decoction itself or the interaction between Si Miao decoction and acupuncture (or cupping). Researchers should find out the possible mechanism of Si Miao decoction in treating gout and the interaction between herbal medicine and acupuncture.
2. The methodology is well-defined for Systematic Review and Meta-analysis; however, the including studies as the materials in this article have many methodological flaws, such as randomization, double-blind and allocation concealment. The results and conclusion could not be judged solidly, so it could not be recommended to TCM practitioners worldwide.
3. More solid and well-defined scientific studies should be included for analysis.

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Partly

Is the statistical analysis and its interpretation appropriate?

Partly

Are the conclusions drawn adequately supported by the results presented in the review?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: traditional Chinese medicine and acupuncture

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 16 April 2021

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Jun Yong Choi

National Clinical Research Center for Korean Medicine, Korean Medicine Hospital of Pusan National University, Yangsan, South Korea

This is a systematic review&meta-analysis of the effect of modified Si Miao decoction combined with acupuncture and cupping therapy compared to western medicine on gout. There are several points to be clear for improving this manuscript.

1. Please add a table for the information of every herb contained in the modified Si Miao decoction in each study. Also, acupuncture points used and specific names of western medicines in the control group in every analysed study should be contained in this table.
2. Safety must be considered when assessing the efficacy of every medical intervention. So, add the information of safety of included studies.
3. From the result of this study, modified Si Miao decoction plus acupuncture and cupping therapy showed significant effects of lowering blood uric acid level as well as ESR and CRP over western medicine. Please provide suggestive mechanisms of these TCM interventions on lowering these biomarkers in the discussion section with relevant references.
4. Also, there should be a note of caution in the manuscript about the use of these TCM interventions against the use of standard therapy of gout before firm clinical evidence of TCM is established.

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Yes

Is the statistical analysis and its interpretation appropriate?

Partly

Are the conclusions drawn adequately supported by the results presented in the review?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Traditional Medicine (eastern asian).

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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