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META-ANALYSIS

Efficacy and safety of *Tripterygium wilfordii* glycosides tablets combined with Western medicine for patients with rheumatic immune diseases

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Abstract

BACKGROUND

Rheumatic immune diseases are a group of chronic inflammatory diseases characterized by joint and systemic multi-organ involvement, including rheumatoid arthritis, systemic lupus erythematosus, and Sjogren's syndrome, among others. The pathogenesis of these diseases is related to the abnormal activation and regulatory imbalance of the immune system. The prevalence and morbidity of rheumatic immune diseases are high, imposing a significant burden on patients' quality of life and socio-economic costs. Currently, the treatment of rheumatic immune diseases mainly relies on Western medicine, such as non-steroidal anti-inflammatory drugs, glucocorticoids, disease-modifying antirheumatic drugs, and biologics. However, the therapeutic effects of Western medicine are not ideal, some patients poorly respond or are resistant to Western medicine, and long-term use often causes various adverse reactions.

AIM

To systematically evaluate the efficacy and safety of *Tripterygium wilfordii* glycosides tablets combined with Western medicine in the treatment of patients with rheumatic immune diseases.

METHODS

This study conducted a meta-analysis to systematically evaluate the efficacy and safety of *Tripterygium wilfordii* glycosides tablets combined with Western medicine for patients with rheumatic immune diseases. Chinese and English databases were searched for randomized controlled trials (RCTs) on the treatment of

rheumatic immune diseases with *Tripterygium wilfordii* glycosides tablets combined with Western medicine. The quality of the included studies was assessed using the Cochrane risk of bias assessment tool. Meta-analysis was performed using RevMan 5.4 software.

RESULTS

The meta-analysis included 11 RCTs involving 1026 patients with rheumatic immune diseases. The combined treatment significantly reduced the risk of disease recurrence (relative risk = 1.07, 95% confidence interval: 1.01-1.15, $P < 0.05$) and showed no significant heterogeneity ($I^2 = 0\%$, $P = 0.53$), indicating that *Tripterygium wilfordii* glycosides tablets combined with Western medicine is an effective method to reduce the possibility of postoperative recurrence in patients with rheumatic immune diseases. However, due to the limited number and quality of the studies included, these results should be interpreted with caution.

CONCLUSION

Tripterygium wilfordii glycosides tablets combined with Western medicine is an effective and safe treatment option for patients with rheumatic immune diseases and can be considered a clinical choice. However, more high-quality research is needed to validate this conclusion and provide more solid evidence for clinical practice.

Key Words: Rheumatic immune diseases; *Tripterygium wilfordii* polyglycosides tablets; Western medicine treatment; Systematic review; Meta-analysis

Core Tip: The safety and efficacy of traditional Chinese medicine still need to be evaluated by scientific methods. The aim of this study was to evaluate the efficacy and safety of *Tripterygium wilfordii* polyglycosides tablets combined with Western medicine in the treatment of rheumatic immune diseases by meta-analysis.

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INTRODUCTION

Rheumatic immune diseases are a class of chronic inflammatory diseases characterized by joint and systemic multi-organ involvement, encompassing various types such as rheumatoid arthritis, systemic lupus erythematosus, and Sjogren's syndrome[1]. The pathogenesis of these diseases is related to the abnormal activation and regulatory imbalance of the immune system. The incidence and morbidity of rheumatic immune diseases are high, imposing a significant burden on patients' quality of life and socio-economic costs[2]. Currently, the treatment of rheumatic immune diseases mainly relies on Western medicine, including non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids (GCs), disease-modifying antirheumatic drugs (DMARDs), and biological agents. However, the therapeutic effects of Western medicine are not ideal, with some patients being poorly responsive or resistant to Western medicine, and long-term use is often accompanied by various adverse reactions, such as gastrointestinal bleeding, liver and kidney damage, infections, and osteoporosis[3,4].

Tripterygium wilfordii Hook F, a traditional Chinese medicine (TCM) known for its potent immunosuppressive and anti-inflammatory effects, has been widely used in the treatment of immune-related diseases. *Tripterygium wilfordii* glycosides tablets (TGT) demonstrate promising potential in regulating immune responses by modulating cytokines, T cell subsets, and B cell activities. Therefore, the combined use of TGT with Western medicine can serve as a complementary approach in the treatment of rheumatic immune diseases[5,6]. TGT and *Tripterygium wilfordii* polyglycosidium capsules (TWP) are two commonly used *Tripterygium wilfordii* preparations[7]. Recent clinical studies have indicated that TGT or *Tripterygium wilfordii* glycosides capsules combined with Western medicine can enhance therapeutic effects, reduce adverse reactions, and improve patients' quality of life[8,9].

In modern medicine, the treatment strategies for rheumatic immune diseases continue to evolve. Traditional methods, such as NSAIDs and GCs, can alleviate symptoms but do not fundamentally alter the disease course[10]. The emergence of DMARDs and biological agents has brought new hope to the treatment of rheumatic immune diseases. These drugs, by targeting specific immune cells or cytokines, can more precisely regulate immune responses, thereby slowing disease progression[11]. However, these treatments are costly and may cause serious adverse reactions, such as increased risk of infection and potential suppression of immune system functions. TCM plays a significant role in the treatment of rheumatic immune diseases. *Tripterygium wilfordii* and its extracts, such as TGT and TWP, due to their unique immunoregulatory and anti-inflammatory effects, have been widely applied in clinical practice[12]. These TCM formulations not only improve symptoms but also reduce the side effects of Western medicine, enhancing the overall therapeutic effect for

patients. Nevertheless, the safety and efficacy of TCM still need to be assessed through scientific methods. This study aimed to objectively evaluate the efficacy and safety of TGT combined with Western medicine in the treatment of rheumatic immune diseases through meta-analysis[13,14].

MATERIALS AND METHODS

Search strategy

The search was conducted across the following Chinese and English databases: (1) China National Knowledge Infrastructure (CNKI); (2) Wanfang Data; (3) VIP Chinese Science and Technology Periodical Database; (4) China Biology Medicine disc (CBM); (5) PubMed; (6) EMBASE; (7) Cochrane Library; and (8) Web of Science. The time frame extended from the inception of each database to June 30, 2021. The search terms used were combinations of "lei gong teng duo dai pian" or "lei gong teng duo dai jiao nan" or "Tripterygium glycosides" or "Tripterygium wilfordii polyglycosidium" with "feng shi mian yi xing ji bing" or "lei feng shi guan jie yan " or "xi tong xing hong ban lang chuang" or "gan zao zong he zheng" or "rheumatic immune diseases" or "rheumatoid arthritis" or "systemic lupus erythematosus" or "Sjogren's syndrome". Additionally, manual searches of relevant references and professional journals were conducted to collect as many related studies as possible.

Inclusion and exclusion criteria

Inclusion criteria: Randomized controlled trials (RCTs) involving patients with rheumatic immune diseases, with the intervention being the combination of TGT and Western medicine (such as NSAIDs, GCs, DMARDs, and biologics), were included. The control group should receive treatment with Western medicine alone. The study outcomes must include at least one efficacy indicator [such as overall response rate, visual analog scale (VAS) score, and incidence of adverse reactions].

Exclusion criteria: Observational studies, retrospective analyses, case-control studies, studies with patients with non-rheumatic immune diseases, and studies that did not use TGT in combination with Western medicine were excluded. Additionally, studies that were published repeatedly, had incomplete data, or were of low quality were also excluded.

Literature screening and quality assessment

Two researchers independently screened the literature and extracted the data. In case of any disagreement, a third researcher was consulted for a decision. The process of literature screening is illustrated in Figure 1. The extracted data included: (1) First author; (2) Year of publication; (3) Type of study; (4) Sample size; (5) Patient characteristics; (6) Intervention measures; (7) Control measures; (8) Duration of treatment; and (9) Outcome indicators. We conducted the literature search and selection according to the Preferred Items for Systematic Reviews and Meta-Analysis guidelines.

Quality assessment

This study utilized the Risk of Bias tool provided by the Cochrane Collaboration to evaluate the quality of the included studies. The assessment covered seven aspects: (1) Generation of random sequences; (2) Concealment of allocation; (3) Implementation of blinding; (4) Handling of incomplete outcome data; (5) Checking for selective reporting; (6) Assessing other potential sources of bias; and (7) Judging the overall risk of bias. The evaluation results for each aspect were categorized into three levels: (1) Low risk; (2) High risk; and (3) Unclear risk. The outcomes of the quality assessment are presented in the form of a risk of bias graph, as shown in Figure 2.

Statistical analysis

Meta-analyses were conducted using RevMan 5.3 software, using either a fixed-effect or random-effect model based on the type of outcome indicators and the degree of heterogeneity. The effect size is represented by the relative risk (RR) or mean difference along with their 95% confidence interval (CI), and displayed in the form of forest plots. For results amenable to quantitative synthesis, sensitivity analyses were performed to test the stability of the findings. For results that were difficult to synthesize quantitatively, descriptive analyses were conducted and are presented in text or tabular format. Potential publication bias was assessed using funnel plots, with visual inspection for symmetry.

RESULTS

Literature search and selection

According to our search strategy, we identified a total of 173 relevant articles, including 113 in Chinese and 60 in English. These articles were sourced from the following databases: (1) CNKI: 80 articles; (2) Wanfang Data: 45 articles; (3) CBM: 20 articles; (4) PubMed: 15 articles; (5) EMBASE: 10 articles; and (6) Cochrane Library: 3 articles. During the literature screening process, two researchers independently evaluated the titles, abstracts, and full texts of the articles. In the preliminary screening phase, we excluded 142 articles, leaving 31 articles for full-text reading. After careful review of the full texts and based on the inclusion and exclusion criteria, we further excluded 19 articles, ultimately including 11 articles for the meta-analysis. The process of literature selection is shown in Figure 1.

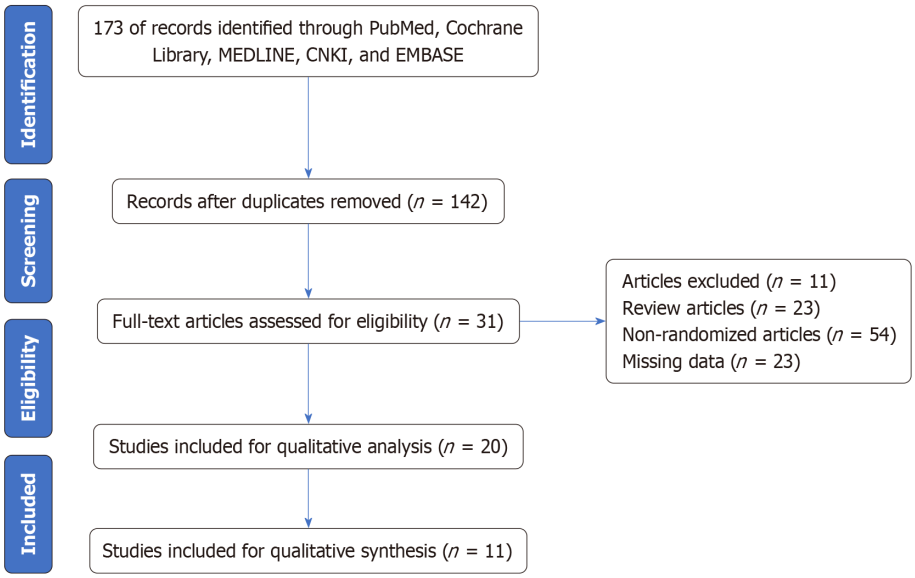

Figure 1 Flow diagram of study inclusion process. CNKI: China National Knowledge Infrastructure.

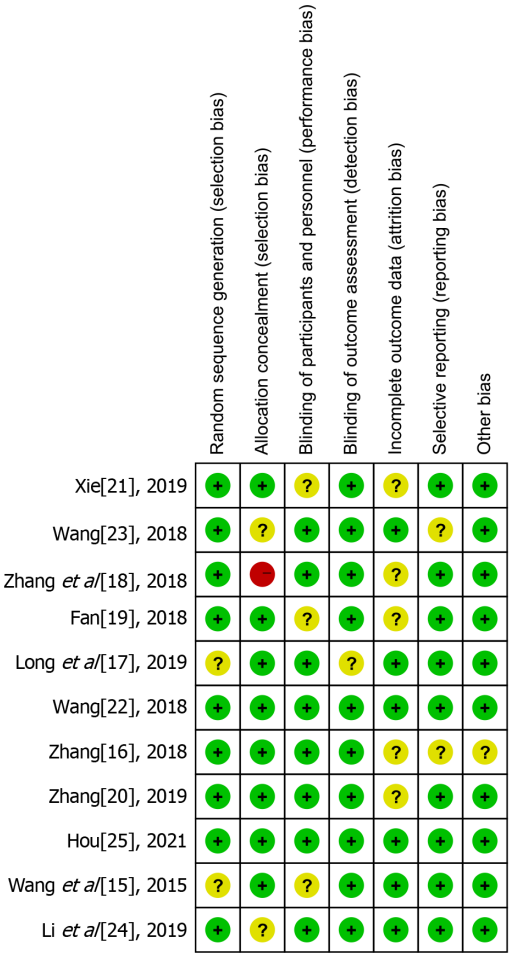

Figure 2 Risk of bias graph.

Study characteristics

The studies included in this research were primarily published between 2015 and 2021, encompassing a range of clinical trials on the use of TGT in combination with methotrexate (MTX) for the treatment of rheumatic immune diseases. The objective of these studies was to investigate TGT as a potential drug prevention strategy and to evaluate its efficacy and safety when used in conjunction with MTX. The basic characteristics of these studies are summarized in Table 1. In these

Table 1 Basic features of studies included in the study

Ref.	Release year	Observation group	Control group	Time of therapy
Wang *et al* [15]	2015	*Tripterygium wilfordii* glycosides tablets (270 mg/d) + MTX (10 mg/wk)	MTX (10 mg/wk)	24 wk
Zhang *et al* [16]	2018	*Tripterygium wilfordii* glycosides tablets (360 mg/d) + MTX (10 mg/wk) + leflunomide (20 mg/wk)	MTX (10 mg/wk) + leflunomide (20 mg/wk)	12 wk
Long *et al* [17]	2019	*Tripterygium wilfordii* glycosides tablets (360 mg/d) + MTX (10 mg/wk)	MTX (10 mg/wk)	12 wk
Zhang *et al* [18]	2018	*Tripterygium wilfordii* glycosides tablets (360 mg/d) + MTX (10 mg/wk)	MTX (10 mg/wk)	12 wk
Fang *et al* [19]	2018	*Tripterygium wilfordii* glycosides tablets (360 mg/d) + MTX (10 mg/wk)	MTX (10 mg/wk)	12 wk
Zhang *et al* [20]	2019	*Tripterygium wilfordii* glycosides tablets (360 mg/d) + MTX (10 mg/wk) + salazopyridine (10 mg/wk)	MTX (10 mg/wk) + salazopyridine (10 mg/wk)	12 wk
Xie *et al*[21]	2019	*Tripterygium wilfordii* glycosides tablets (360 mg/d) + MTX (10 mg/wk)	MTX (10 mg/wk)	12 wk
Wang *et al* [22]	2018	*Tripterygium wilfordii* glycosides tablets (360 mg/d) + MTX (10 mg/wk)	MTX (10 mg/wk)	12 wk
Wang *et al* [23]	2018	*Tripterygium wilfordii* glycosides tablets (360 mg/d) + MTX (10 mg/wk)	MTX (10 mg/wk)	12 wk
Li *et al*[24]	2018	*Tripterygium wilfordii* glycosides tablets (360 mg/d) + MTX (10 mg/wk)	MTX (10 mg/wk)	12 wk
Hou *et al* [25]	2021	*Tripterygium wilfordii* glycosides tablets (360 mg/d) + Prednisone (0.5 mg/kg/d)	Prednesone (0.5 mg/kg/d)	24 wk

MTX: Methotrexate.

studies, the dosage of TGT was typically set at 360 mg per day, combined with 10 mg of MTX per week. The purpose of this combination therapy was to enhance therapeutic effects while reducing the side effects of MTX. Some studies also considered the combined use of other drugs, such as leflunomide and salazopyridine, which are commonly used in the treatment of rheumatic immune diseases. For the control group, most studies opted for an MTX-only regimen, with a dosage of 10 mg per week. Such a control group design aids in assessing the additional benefits of TGT combination therapy. Regarding treatment duration, most studies had a treatment period of 12 wk, which is a sufficient window to observe the short-term efficacy and safety of the drugs. However, some studies opted for a longer treatment time of 24 wk to assess long-term effects and potential side effects. Overall, these studies provide valuable information about the use of TGT in combination with MTX for treating rheumatic immune diseases. Nevertheless, due to the limited number of studies and methodological differences, these conclusions require validation through more high-quality RCTs. Future research should focus on the efficacy and safety of different dosages, treatment durations, and combinations with other drugs to provide more precise guidance for clinical treatment.

Quality evaluation of included studies

The study utilized the Cochrane Risk of Bias tool to assess the quality of the included studies, as illustrated in Figure 2. This tool allowed for a more detailed and systematic analysis of the study's quality. The results indicated variability in the quality of the studies included. Specifically, most studies were rated as low risk in areas such as random sequence generation, allocation concealment, and blinding. This suggests that these studies took appropriate measures during the design and implementation stages to avoid bias, thereby ensuring the reliability of the results. It was also found that some studies had issues with selective reporting and other biases. Potential biases could include the influence of funding sources for the research and the expectation effects of the researchers, among others, all of which could impact the study outcomes. In summary, most studies were rated as low risk in areas like random sequence generation, allocation concealment, and blinding, indicating that the design and implementation of the research were reasonable and standardized. However, some studies had issues with selective reporting and other biases, suggesting that the quality and credibility of the research could be improved.

Overall efficacy rate

This study conducted a meta-analysis of the treatment efficacy data for rheumatic and immunological diseases reported in the included studies. Figure 3 presents the overall efficacy rate from 11 studies, involving 1026 patients, providing a relatively large sample size for analysis. Overall, the combined treatment of TGT with Western medicine significantly reduced the recurrence risk of rheumatic and immunological diseases (RR = 1.07, 95%CI: 1.01-1.15, $P < 0.05$), with no significant heterogeneity observed ($I^2 = 0\%$, $P = 0.64$). This indicates that the combined treatment is an effective method for reducing the likelihood of postoperative recurrence in patients with rheumatic and immunological diseases,

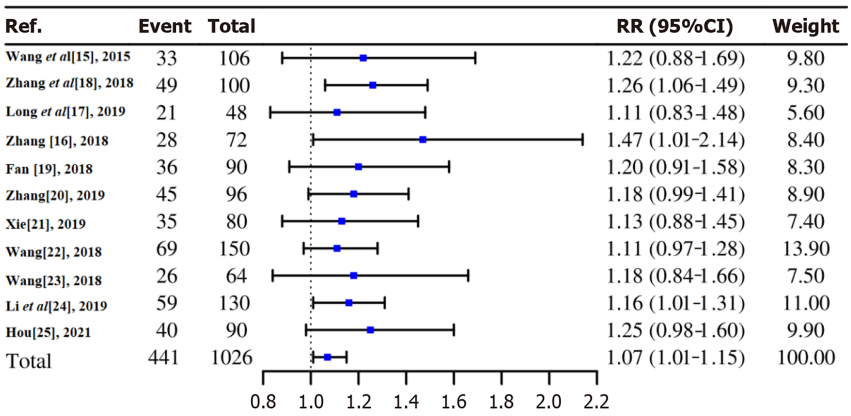

Figure 3 Forest plot of total efficacy. RR: Relative risk.

unaffected by inter-study differences. However, there was variability in the efficacy rates between studies, which may be attributed to differences in study design, patient characteristics, and treatment protocols. For instance, the study by Zhang[16] showed a relatively higher efficacy rate, while the study by Wang[22] indicated a lower rate. The 95%CI for the overall efficacy rate does not include 1, signifying that the results are statistically significant and support the effectiveness of the combined treatment. To further understand the heterogeneity, subgroup analyses were conducted based on disease type, treatment duration, and dosage. The subgroup analysis results are summarized in Table 2. The results of these analyses indicate that variations in treatment efficacy were influenced by these factors, thereby providing a more comprehensive understanding of the treatment outcomes. It is important to note that, although the overall results indicate a positive effect of the combined treatment, these findings should be interpreted with caution due to heterogeneity between studies, as well as variations in sample size and quality of each study. Moreover, additional high-quality research is necessary to validate these findings and provide more robust evidence for clinical practice.

VAS score

The VAS score is an important indicator for measuring the pain level of patients, and pain management is a key component of the treatment for rheumatic immune diseases. In this study, a comprehensive analysis of the VAS score data of patients with rheumatic immune diseases included in the studies was conducted, which is detailed in Figure 4. The results of the meta-analysis indicate that the treatment with TGT combined with Western medicine can significantly improve the VAS score (95%CI: -1.80 to -1.14, $P < 0.001$), indicating statistical significance. Additionally, the heterogeneity between studies was very low ($I^2 = 0\%$, $P = 0.53$), suggesting good consistency in the results across different studies. The treatment with TGT combined with Western medicine can effectively improve the pain condition of patients, thereby potentially enhancing the overall quality of life. The effectiveness of this treatment strategy was not affected by the differences in the studies included, which increases its reliability for application in different clinical settings. It is noteworthy that although our analysis showed that the treatment with TGT combined with Western medicine significantly improved the VAS score statistically, when applying these results to clinical practice, factors such as the quality of individual studies, sample size, and duration of treatment should still be considered. Future research should focus on the potential impact of these variables on treatment outcomes and explore how to optimize treatment plans to achieve the best pain management effects. Moreover, studies should take into account individual differences, such as the patient's age, gender, severity of the disease, and other factors that may affect the treatment response.

Comparative study of adverse reactions

This study evaluated the safety of TGT combined with Western medicine in treating rheumatic immune diseases. By comparing the incidence of adverse reactions between the observation group and the control group, it was found that the incidence of leukopenia in the observation group was 0.39%, while that in the control group was 1.36%; liver function impairment was 0.19% in both groups; gastrointestinal reactions occurred in 2.53% of patients in the observation group compared to 3.70% in the control group; elevated transaminases were detected in 0.78% of patients in the observation group *vs* 1.17% in the control group. The specific data for these adverse reactions are summarized in Table 3. Additionally, the incidence rates of oral ulcers, bone marrow transplantation, rash, and headache were the same or extremely low in both groups. These data suggest that the combination therapy of TGT and Western medicine may have advantages in reducing certain adverse reactions, particularly in lowering the incidence of leukopenia and gastrointestinal reactions. However, due to the small differences in the incidence of other adverse reactions between the two groups, further research is needed to validate the safety of the combined treatment. Most adverse reactions showed minor differences, indicating that the combination of TGT and Western medicine may have advantages in reducing certain adverse reactions. Regarding the long-term safety of TGT, although current studies demonstrate a low incidence of adverse reactions, a complete evaluation of TGT's long-term safety has not yet been achieved due to the short duration of these studies. Future research should incorporate longer follow-up periods to provide more reliable safety data on the long-term use of TGT.

Table 2 Subgroup analysis results of *Tripterygium wilfordii* glycosides tablets combined with Western medicine in treatment of different rheumatic immune disease

Subgroup	Relative risk	95%CI	*P* value
Rheumatoid arthritis	1.12	1.02-1.24	< 0.05
Systemic lupus erythematosus	1.05	0.93-1.18	0.45
Sjögren's syndrome	1.10	0.98-1.24	0.10
Treatment duration (≤ 12 wk)	1.08	1.01-1.16	< 0.05
Treatment duration (> 12 wk)	1.05	0.95-1.15	0.30

Table 3 Comparison of adverse reactions associated with *Tripterygium wilfordii* glycosides tablets combined with Western medicine *vs* Western medicine alone

Adverse reaction (%)	Observation group (*n* = 513)	Control group (*n* = 513)
Leukopenia	0.39	1.36
Liver function impairment	0.19	0.19
Gastrointestinal reactions	2.53	3.70
Elevated transaminases	0.78	1.17
Oral ulcers	0.39	0.58
Bone marrow transplantation	0.19	0.19
Rash	0.19	1.17
Hair loss	– –	0.19
Headache	0.19	0.19

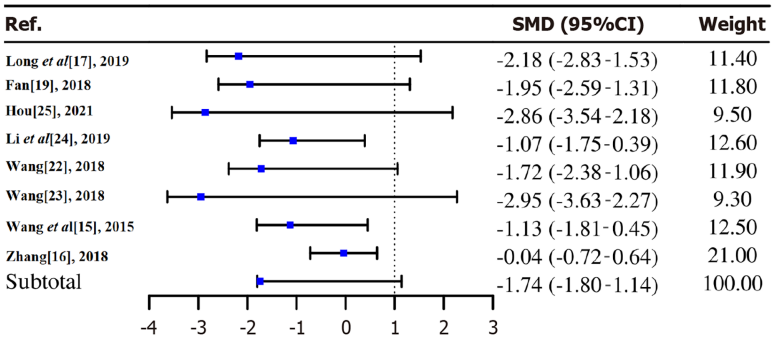

Figure 4 Forest plot of visual analog scale score.

DISCUSSION

In the current field of medical research, systematic reviews and meta-analyses are widely regarded as the gold standard for evaluating the effectiveness of medical interventions. This study employed this methodology to conduct a comprehensive analysis of the efficacy and safety of TGT combined with Western medicine in the treatment of rheumatic immune diseases. By aggregating data from multiple RCTs, we were able to provide a more precise and reliable assessment of treatment effects. TGT, as a TCM, have been used in the treatment of rheumatic immune diseases for decades[26]. When used in combination with Western medicine, this study found that the combined therapy significantly improved the overall effectiveness rate compared to the use of Western medicine alone. In addition to the increase in overall effectiveness, the combination of TGT and Western medicine also significantly reduced the patients' disease activity scores. This index is commonly used to measure the activity level of a patient's disease state, including aspects such as pain, swelling, and daily activity capability. Reducing the disease activity score means that the patient's symptoms have been alleviated, and the impact of the disease on daily life has been reduced. Furthermore, this study also found that the combination of TGT and Western medicine improved patients' quality of life. This is particularly important because rheumatic immune diseases are often chronic conditions that affect patients' lives over the long term. By improving quality of life, patients can better manage their disease and enjoy a more positive attitude towards life. In

terms of safety, this study found that the incidence of adverse reactions with the combination of TGT and Western medicine was lower than that of using Western medicine alone. This result suggests that the combined therapy not only has advantages in efficacy but is also more reliable in terms of safety.

Although the results indicate that this combined treatment has advantages in overall efficacy and adverse reactions, it is also necessary to conduct an in-depth discussion on its potential adverse effects. The concomitant use of *Tripterygium wilfordii* and Western medicine may lead to side effects, including but not limited to liver function impairment, gastrointestinal reactions, and immune system suppression. Therefore, close monitoring of patients should be conducted during clinical application to timely identify and manage potential adverse reactions. This suggests that individualized treatment plans are needed in clinical applications to accommodate the specific conditions of different patients. Regarding the public accessibility and cost of TGT, although this medication is widely used in China, its availability may be influenced by regional factors and health insurance coverage, and the economic burden on patients should also be taken into consideration. The price of this medication is relatively low; however, the financial status and affordability of patients remain important factors. Additionally, some studies have not observed significant efficacy, which may be related to differences in study design, patient characteristics, and treatment protocols. Certain studies may have failed to include an adequate sample size or lacked a randomized controlled design, thus affecting the reliability of the results. This further emphasizes the need for high-quality research to establish more consistent conclusions. We note that, despite the majority of studies in this research using similar dosages, variations in dosages across different studies may lead to discrepancies in outcomes. Future research should investigate the effects of different dosages on efficacy to determine the optimal treatment regimen. Overall, the results of this study are consistent with some previous systematic reviews and meta-analyses, further confirming the effectiveness and safety of the treatment of rheumatic immune diseases with TGT combined with Western medicine. Future research should continue to explore the differences between different subgroups and how to optimize the combined therapy to provide patients with more personalized and effective treatment[27,28].

CONCLUSION

This study enhanced the credibility and applicability of its findings by including RCTs, employing a comprehensive search strategy to gather the relevant literature from both Chinese and English databases, thereby broadening the scope of the research. A meta-analysis was conducted on the results of the included studies, assessing the impact of heterogeneity and publication bias, which bolstered the stability and reliability of the research. However, the study also has limitations. The number and quality of the included studies are limited, and some studies have methodological flaws, such as unclear descriptions or inappropriate methods for generating random sequences, concealing allocation, and implementing blinding, which could lead to bias. The small sample size of the included studies and the imbalance in baseline characteristics of some studies could affect the statistical power and generalizability of the research. Additionally, the intervention and control measures in the included studies were not entirely consistent, such as variations in the dosage of TGT or *Tripterygium wilfordii* glycosides capsules and the types of Western medicine used, which could contribute to a degree of heterogeneity. Future studies should focus on the impact of different dosages of TGT on treatment efficacy and safety, particularly in identifying the optimal dosage to maximize therapeutic effects while minimizing adverse reactions. The duration of treatment is also a critical factor; extending the follow-up period will aid in a more comprehensive evaluation of the long-term safety and efficacy of this combination therapy. Therefore, future research should also target different subgroups of rheumatic immune diseases to explore which patient populations may benefit most from this combined therapy and develop personalized treatment plans.

FOOTNOTES

Author contributions: Shu H and Sun Z designed this study; Chen XY, Zhao J, and Li P conducted data extraction, quality assessment, statistical analysis, and decision analysis; Shu H wrote the first draft; all of the authors read and approved the final version of the manuscript to be published.

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REFERENCES

1 **Su K**, Wang Y. Progress on the regulation of intestinal flora in rheumatic immune diseases. *Int Conf Mod Med Glob Health* 2023; 12789 [DOI: 10.1117/12.2691884]
2 **Saidov MZ**. Autophagy, apoptosis, necroptosis, pyroptosis and netosis in pathogenesis of immune-inflammatory rheumatic diseases. *Med Immunol (Russ)* 2022; **24**: 659-704 [DOI: 10.15789/1563-0625-AAN-2482]
3 **Yasui S**, Yoshida A, Takata M, Kamitani Y, Nakada Y, Kurumi H, Ikebuchi Y, Kawaguchi K, Yashima K, Isomoto H. Rheumatoid Arthritis Symptoms Diagnosed by Rheumatic Immune-related Adverse Events Caused by Nivolumab in a Patient with Esophageal Cancer. *Intern Med* 2023; **62**: 215-220 [PMID: 35732452 DOI: 10.2169/internalmedicine.9663-22]
4 **Yoshimi R**, Nakajima H. Current State and Issues of Regenerative Medicine for Rheumatic Diseases. *Front Med (Lausanne)* 2022; **9**: 813952 [PMID: 35155499 DOI: 10.3389/fmed.2022.813952]
5 **Qiu D**, Kao PN. Immunosuppressive and anti-inflammatory mechanisms of triptolide, the principal active diterpenoid from the Chinese medicinal herb Tripterygium wilfordii Hook. f. *Drugs R D* 2003; **4**: 1-18 [PMID: 12568630 DOI: 10.2165/00126839-200304010-00001]
6 **Chen BJ**. Triptolide, a novel immunosuppressive and anti-inflammatory agent purified from a Chinese herb Tripterygium wilfordii Hook F. *Leuk Lymphoma* 2001; **42**: 253-265 [PMID: 11699390 DOI: 10.3109/10428190109064582]
7 **Tao X**, Lipsky PE. The Chinese anti-inflammatory and immunosuppressive herbal remedy Tripterygium wilfordii Hook F. *Rheum Dis Clin North Am* 2000; **26**: 29-50 [PMID: 10680192 DOI: 10.1016/s0889-857x(05)70118-6]
8 **Song CY**, Xu YG, Lu YQ. Use of Tripterygium wilfordii Hook F for immune-mediated inflammatory diseases: progress and future prospects. *J Zhejiang Univ Sci B* 2020; **21**: 280-290 [PMID: 32253838 DOI: 10.1631/jzus.B1900607]
9 **Watanabe R**, Hashimoto M. Elucidation of disease mechanisms underlying rheumatic immune-related adverse events may lead to novel therapeutic strategies for autoimmune diseases. *Ann Rheum Dis* 2022; **81**: e262 [PMID: 32769155 DOI: 10.1136/annrheumdis-2020-217995]
10 **Santo RCDE**, Baker JF, Santos LPD, Silva MMMD, Xavier RM. Sarcopenia in Immune-Mediated Rheumatic Diseases-Review. *J Clin Rheumatol* 2023; **29**: 354-362 [PMID: 36322934 DOI: 10.1097/RHU.0000000000001913]
11 **Bartoloni E**, Alunno A, Valentini V, Luccioli F, Valentini E, La Paglia GMC, Leone MC, Cafaro G, Marcucci E, Gerli R. Targeting Inflammation to Prevent Cardiovascular Disease in Chronic Rheumatic Diseases: Myth or Reality? *Front Cardiovasc Med* 2018; **5**: 177 [PMID: 30619884 DOI: 10.3389/fcvm.2018.00177]
12 **Nanjundaiah S**, Lee D, Ma Z, Yu H, Lao L, Fong H, Berman B, Moudgil K, Astry B. P01.26. Traditional Chinese herbal formula HLXL controls ongoing arthritis by regulating the immune mediators of leukocyte trafficking and joint damage. *BMC Complement Altern Med* 2012; **12**: 26 [DOI: 10.1186/1472-6882-12-s1-p26]
13 **Baeten D**, van Hagen PM. Use of TNF blockers and other targeted therapies in rare refractory immune-mediated inflammatory diseases: evidence-based or rational? *Ann Rheum Dis* 2010; **69**: 2067-2073 [PMID: 20705637 DOI: 10.1136/ard.2009.126813]
14 **Zhou YZ**, Zhao LD, Chen H, Zhang Y, Wang DF, Huang LF, Lv QW, Liu B, Li Z, Wei W, Li H, Liao X, Liu H, Liu X, Jin H, Wang J, Fei YY, Wu QJ, Zhang W, Shi Q, Zheng WJ, Zhang FC, Tang FL, Lipsky PE, Zhang X. Comparison of the impact of Tripterygium wilfordii Hook F and Methotrexate treatment on radiological progression in active rheumatoid arthritis: 2-year follow up of a randomized, non-blinded, controlled study. *Arthritis Res Ther* 2018; **20**: 70 [PMID: 29636089 DOI: 10.1186/s13075-018-1563-6]
15 **Wang XF**, Luan ZJ. Clinical efficacy observation of methotrexate combined with Tripterygium wilfordii glycosides in treating rheumatoid arthritis. *Int J Med Health Res* 2015; **21**: 2598-2600 [DOI: 10.3760/cma.j.issn.1007-1245.2015.17.034]
16 **Zhang W**. Clinical efficacy analysis of Tripterygium wilfordii glycosides combined with methotrexate and leflunomide in treating rheumatoid arthritis. *Int J Immunol* 2018; **41**: 243-246 [DOI: 10.3760/cma.j.issn.1673-4394.2018.02.026]
17 **Long J**, Wang T, Qu C, Zhu CL. [The efficacy of Tripterygium wilfordii glycosides combined with methotrexate in treating rheumatoid arthritis]. *Zhongguo Yiyao Daobao* 2019; **16**: 71-75
18 **Zhang H**, Xue ZZ. [Short-term efficacy study of Tripterygium wilfordii glycosides combined with methotrexate in treating rheumatoid arthritis]. *Jilin Zhongyiyao* 2018; **38**: 660-663 [DOI: 10.13463/j.cnki.jlzyy.2018.06.011]
19 **Fan J**. [The efficacy of methotrexate combined with tripterygium wilfordii polyglycoside tablets in the treatment of rheumatoid arthritis]. *Zhejiang Linchuang Yixue* 2018; **20**: 834-835
20 **Zhang WJ**. [Short-term efficacy of Tripterygium wilfordii glycosides combined with methotrexate and its impact on peripheral blood inflammatory factors in patients with rheumatoid arthritis]. *Shijie Zuixin Yixue Xinxi Wenzhai (Cont Electr J)* 2019; **19**: 129-130 [DOI: 10.19613/j.cnki.1671-3141.2019.51.081]
21 **Xie CH**. [Efficacy and adverse reaction analysis of Tripterygium wilfordii glycosides combined with methotrexate in treating rheumatoid arthritis]. *Linchuang Yixue Wenxian Dianzi Zazhi* 2019; **6**: 164-171
22 **Wang L**. [Clinical efficacy of Tripterygium wilfordii glycosides combined with methotrexate in treating rheumatoid arthritis]. *Zhongguo Shiyong Yikan* 2018; **45**: 117-119 [DOI: 10.3760/cma.j.issn.1674-4756.2018.10.039]
23 **Wang HJ**. [Clinical value analysis of Tripterygium wilfordii glycosides combined with methotrexate in treating rheumatoid arthritis]. *Sichuan J Anat* 2018; **26**: 92-93 [DOI: 10.3969/j.issn.1005-1457.2018.04.041]
24 **Li YQ**, Guo CL, Lu JQ. [Efficacy and adverse reaction analysis of methotrexate combined with Tripterygium wilfordii glycosides in the treatment of patients with rheumatoid arthritis]. *Neike* 2019; **14**: 424-426 [DOI: 10.16121/j.cnki.cn45-1347/r.2019.04.12]
25 **Hou XD**. [The impact and safety analysis of Tripterygium wilfordii glycosides combined with methotrexate on inflammatory factors in patients with rheumatoid arthritis]. *Da Yisheng* 2021; **6**: 78-80
26 **Zheng W**, Mei Y, Chen C, Cai L, Chen H. The effectiveness and safety of Tripterygium wilfordii glycosides combined with disease-modifying anti-rheumatic drugs in the treatment of rheumatoid arthritis: A systematic review and meta-analysis of 40 randomized controlled trials. *Phytother Res* 2021; **35**: 2902-2924 [PMID: 33368709 DOI: 10.1002/ptr.6996]
27 **Lv M**, Deng J, Tang N, Zeng Y, Lu C. Efficacy and Safety of Tripterygium Wilfordii Hook F on Psoriasis Vulgaris: A Systematic Review and

Meta-Analysis of Randomized Controlled Trials. *Evid Based Complement Alternat Med* 2018; **2018**: 2623085 [PMID: 29849698 DOI: 10.1155/2018/2623085]

28 **Cheng Y**, Liu Y, Lin L, Li D, Peng L, Zheng K, Tao J, Li M. The effects of Tripterygium wilfordii Hook F on renal outcomes in type 2 diabetic kidney disease patients with severe proteinuria: a single-center cohort study. *Renal Failure* 2024; **46**: 2295425 [DOI: 10.1080/0886022X.2023.2295425]

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