ISSN 2706-6819 Vol.4, Issue 8: 72-78, DOI: 10.25236/IJFM.2022.040812

Systematic evaluation of efficacy and safety of Biqi capsule in the treatment of ankylosing spondylitis

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Abstract: *Background: At present, the treatment of Ankylosing spondylitis (AS) with Traditional Chinese medicine has attracted wide attention. There are different reports on the efficacy of Biqi capsule in the treatment of AS. Therefore, this study systematically evaluated the effectiveness of Biqi capsule or combined conventional treatment of AS, BASDAI, BASFI, C-reactive protein (CRP), and the occurrence of adverse reactions for meta-analysis. [Methods]: Randomized controlled trials of Biqi capsules or combined conventional treatment of AS were searched in 8 databases including CNKI, VIP, Wanfang Data, CBM, PubMed, Web of Science, Embase and Cochrane Library from July 2022. The effect rate of BIqi capsule on AS, BASDAI score, BASFI score, CRP and the occurrence of adverse reactions were evaluated by random effect model system. [Results]: Seven studies were included with 582 participants, 291 in the treatment group and 291 in the control group. Compared with the control group, the effective rate of BIqi capsule or combined conventional treatment of AS drugs was significantly improved, BASDAI score and BASFI score were significantly reduced, and CRPand adverse reactions had no significant difference. [Conclusion]: Biqi capsule is safe and effective in the treatment of AS, and can significantly improve the activity function.*

Keywords: *Biqi capsule; Ankylosing spondylitis; AS. Meta analysis; Efficient*

1. Introduction

Ankylosing spondylitis (AS) is an early disease with sacroiliac joint lesions, mainly injuries of the axial bones, such AS the spine, sacroiliac joints and spinal attachment points, leading to progressive loss of joint function, chronic back pain and spinal mobility disorders AS the main clinical manifestations [1-2]. AS is an immune-mediated inflammatory disease, with a prevalence of 1‰ to 3‰ in the general population, mainly occurring in young men. The specific pathogenesis of AS is unknown, and the main pathogenic factors include infection, environment, genetic susceptibility, etc. [3-4].AS belongs to the category of "bi disease" in TCM, and TCM has accumulated a lot of experience in long-term treatment practice. Traditional Chinese medicine will be attributed to AS "big hunchback", that the pathogenesis lies in liver and kidney deficiency, invasion of external evil, phlegm and blood stasis mutual knot, vein block, bones and muscles loss. Biqi capsule has the effects of dispelling wind, clearing collasals and nourishing qi, and is used for the treatment of osteoarthritis, rheumatoid arthritis, lumbar muscle strain and some soft tissue injuries caused by other reasons [5]. It is found that there are more and more studies on the use of Biqi capsule in the treatment of AS in China, but the efficacy of patients is different. However, few systematic reviews or meta-analyses of clinical randomized controlled trials of Biqi capsule in the treatment of AS have been reported so far [5-11], so it is necessary to systematically evaluate the literature. At present, most of the clinical studies are small sample studies, so it is necessary to systematically collect and summarize the efficacy and adverse reactions of this drug in clinical application, and re-evaluate the efficacy and safety of this drug by evidence-based medicine method, so as to provide evidence-based basis for clinical treatment and use of this drug.

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2. Methods

We conducted this study according to the guidelines in the Cochrane Handbook of Systematic Intervention Review, version 5.3.0, and reported the results based on systematic reviews and meta-analyses.

2.1 Search Policies

Eight databases including CNKI, VIP, Wanfang Data, CBM, PubMed, Web of Science, Embase and Cochrane Librarywere searched systematically. Chinese and English literatures from the establishment of the database to July 2022 were searched and the following Chinese keywords were used in (CNKI, VIP, Wanfang Data, CBM) :(biqi capsule) and (ankylosing spondylitis, randomized control, randomized allocation, etc.). Keywords used in English databases (PubMed, Web of Science, Embase, Cochrane Library) include (Biqi capsule, Biqi) and (AS, Ankylosing spondylitis, random Clinical trail)

2.2 Inclusion study

The study was selected for inclusion by two independent reviewers (Liang Zhuang and Yang Lei) and approved by the corresponding author (Dong Bo). The process of research selection is shown in Table 1. Studies that meet PICOS (Participant, Intervention, Comparator, Outcome, and Study Design) criteria. Inclusion criteria :(1) this study was a randomized controlled clinical trial; (2) Participants must have primary AS; (3) The treatment group in this study was Biqi capsule or combined with conventional treatment AS drugs; 4) This study included response rate, BASDAI, BASFI, C-reactive protein (CRP) and one of the adverse reactions as outcome indicators.

2.3 Exclusion Study

Exclusion criteria :(1) non-chinese randomized controlled trials. (2) Animal experimental study. (3) Letters, conference abstracts, case reports, reviews, critical papers. (4) There were no control group intervention studies. (5) Secondary AS. (6) The average or variance results before and after the experiment were not completely recorded.

2.4 Data extraction and quality assessment

Two investigators (Liang Zhuang and Yang Lei) independently extracted detailed information from each included study using a standardized template. For example, the first author, publication year, age, course of disease, sample size, study design, intervention measures of experimental group and control group, treatment dose and frequency of Biqi capsule and control group, treatment course, and outcome indicators. (See Table 1)

The authors independently assessed the study quality and risk of bias for each eligible study using criteria outlined in the Cochrane manual (higgins and Altman2008). Six criteria were considered (see figure 1) :(1) random sequence distribution generation; (2) Distribution hiding; (3) blind method; (4) Result data; (5) Selective reporting; (6) Other biases. The studies were classified as high risk, low risk or no clearance. When there is disagreement, we follow the advice of an independent researcher (Dong Bo). The dichotomous variables were represented by odds ratio (OR), and the continuous variables were represented by weighted mean difference (WMD). Each effect size was represented by 95% confidence interval (CI). The I2 test was used to analyze the heterogeneity of the included studies. When the heterogeneity among the studies was small (I2 ≤50% and P > 0.1), the fixed-effect model was used. When heterogeneity was large (I2 > 50% and P≤0.1), a random-effect model was used to conduct subgroup analysis to find the source of heterogeneity. If the number of literatures was ≥10, potential publication bias was assessed by funnel plot analysis. It was quantitatively evaluated using Egger and Bgger tests. Sensitivity analysis was used to assess publication bias.

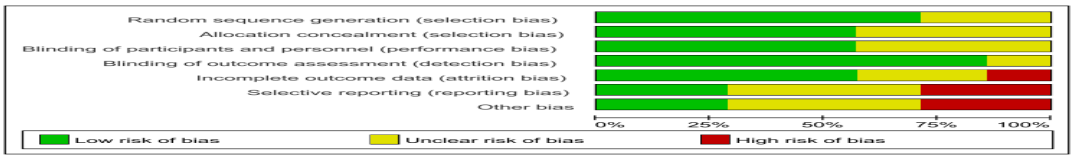

Figure 1: Risk Assessment table

ISSN 2706-6819 Vol.4, Issue 8: 72-78, DOI: 10.25236/IJFM.2022.040812

3. The results

The flow chart of literature retrieval is shown in Figure 2. A total of 247 articles were collected from 8 databases including CNKI, VIP, Wanfang Data, CBM, PubMed, Web of Science, Embase and Cochrane Library. 69 duplicated articles were deleted, 106 were deleted by title and abstract screening, including 62 non-randomized controlled trials, 14 review papers, 12 animal studies, and 18 with incomplete results. After reading the full text, a total of 72 articles were included, 65 records were deleted. Seven papers that met the criteria were included in the meta-analysis

3.1 Research characteristics and literature quality evaluation

The basic characteristics of the included studies are shown in Table 1. In seven studies. The study years were from 2012 to 2022. Sample sizes ranged from 40 to 140. A total of 582 people were divided into treatment or control groups. The duration of the disease ranged from three to eight years. Six patients were treated for 12 weeks and one was treated for 4 weeks. Patients in three of the studies were <30 years old, between 30 and 40 years old, and one was >40 years old. (Study of risk bias) According to the Cochrane Manual, our risk bias assessment results are shown in Figure 1. A total of 7 literatures were included in this study, among which 1 used random number method, 51 mentioned random number using envelope lottery method, 1 used random throwing method, and the remaining 4 only mentioned random grouping without detailed description of methods, so it is impossible to judge the correctness of randomness and randomness has a high risk of bias. None of the studies mentioned blindness, which is risky. None of the 7 articles mentioned whether blind method and distribution concealment were used, and 2 mentioned follow-up, without loss of follow-up bias or other bias. Therefore, a risk bias assessment tool was used to evaluate the quality of the included studies.

3.2 Effectiveness and safety analysis of treatment group and control group

3.2.1 Efficient

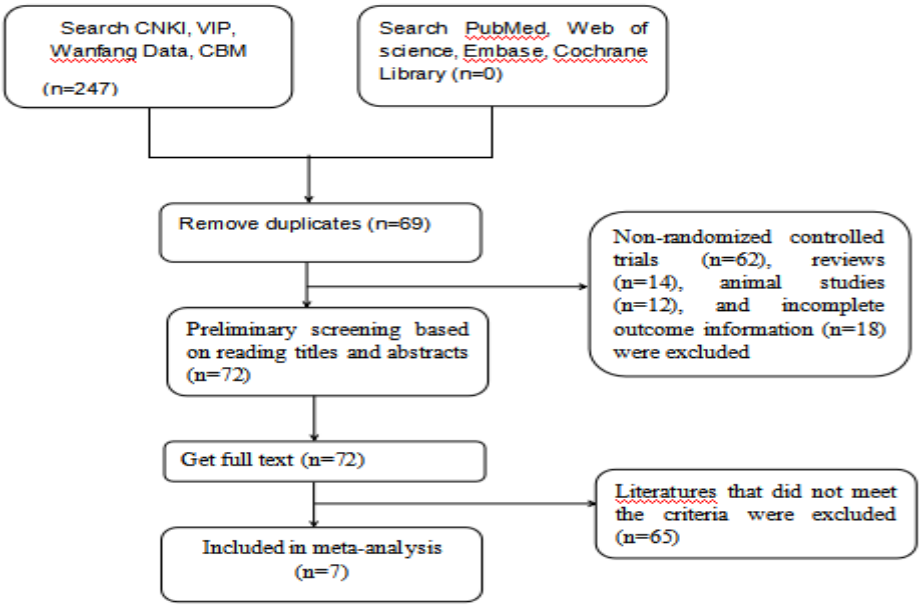

Figure 2: Flow chart of literature screening

A meta-analysis of effectiveness was conducted in 17 literatures (Figure 3), and it was found that biqi capsule or combined with conventional treatment had a significant increase in clinical efficacy (RR) of 1.18 (95%CI: 1.03,1.37; I2 =0.0%, P =0.907). Heterogeneity is small, there is no publication bias, and the results are robust.

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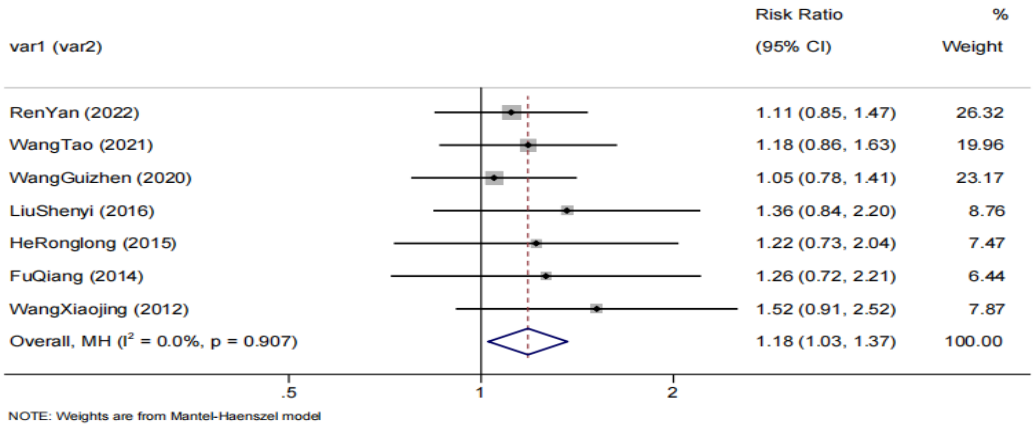

Figure 3: Efficiency

3.2.2 Basdai score

Five literatures were included (FIG. 4) to study the changes of BASDAI score, and it was found that the BASDAI score after BIqi capsule or combined with conventional treatment decreased significantly (SMD: -2.30) (95% CI: -2.61, -2.00; I2 =98.1%, P =0.000). High heterogeneity. Egger (P=0.195>0.05), begg (P=0.221>0.05), there was no publication bias, the results were robust.

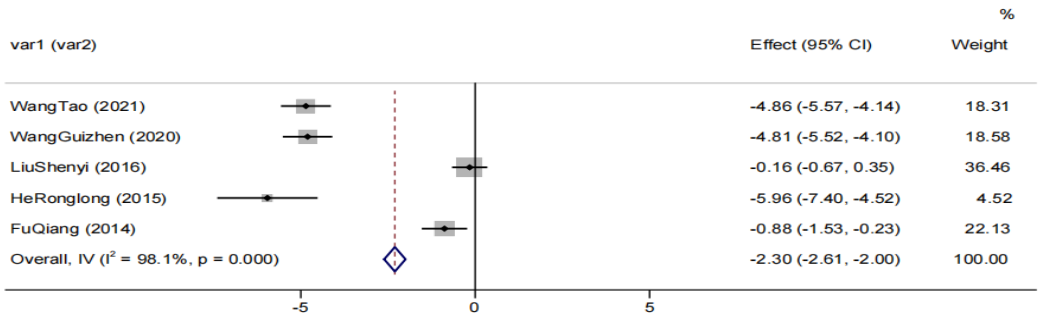

Figure 4: BASDAI score

3.2.3 Basfi score

Five literatures were included (FIG.5) to study the changes of BASFI score, and it was found that the BASFI score (SMD) of Biqi capsule or combined with conventional treatment was significantly lower than that of conventional treatment (-2.17) (95% CI: -2.55, -1.97; I2 =99.0%, P =0.000). High heterogeneity. Egger (P=0.01<0.05), begg (P=0.221>0.05), there is publication bias, the results are not robust

3.2.4 CRP

Five studies were included (FIG.6) to study CRP changes, and it was found that biqi capsule or combined with conventional treatment had no significant change in CRP (SMD) after AS drug treatment (0.39) (95%CI: 0.16, 0.62; I2 =97.8%, P =0.000). High heterogeneity and publication bias.

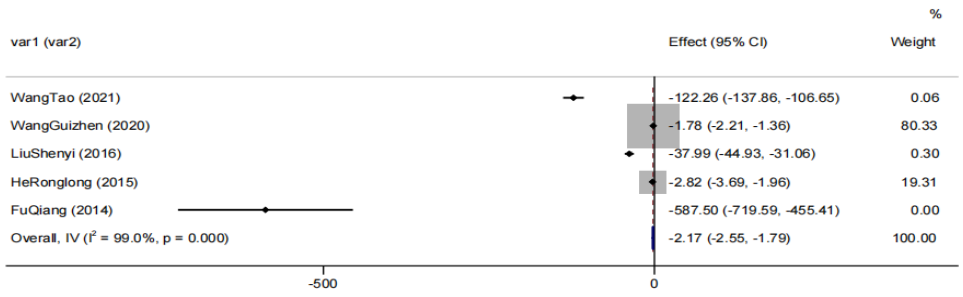

Figure 5: BASFI score

ISSN 2706-6819 Vol.4, Issue 8: 72-78, DOI: 10.25236/IJFM.2022.040812

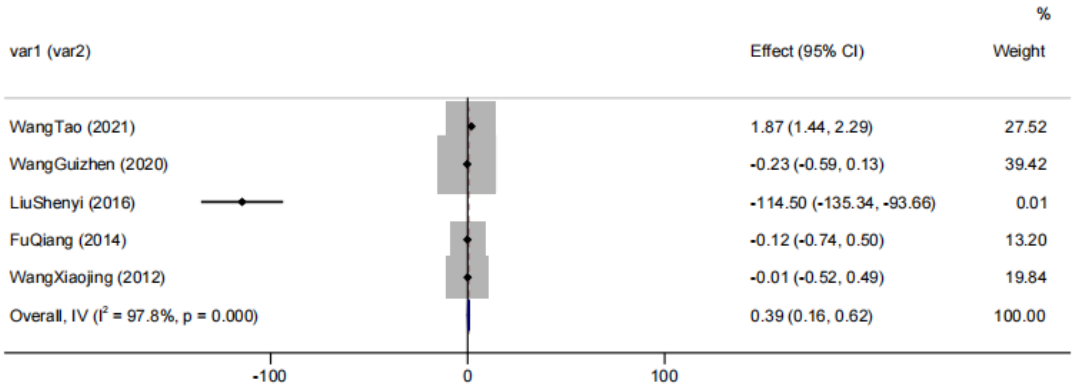

Figure 6: CRP

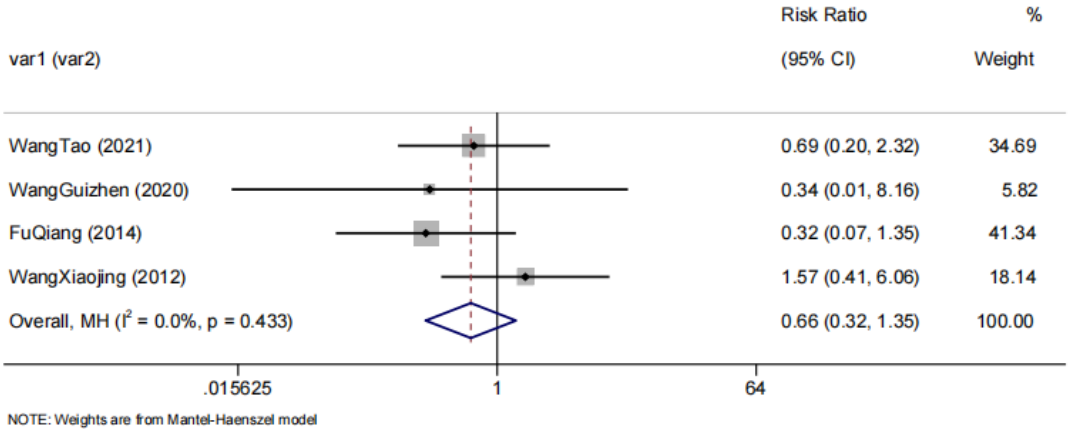

Figure 7: Adverse reactions

3.2.5 Adverse reactions

Five literatures were included (FIG. 7) to study the changes of adverse reactions, and it was found that biqi capsule or combined with conventional treatment had no significant change in the incidence of adverse reactions (RR) after AS drug treatment compared with conventional treatment (RR: 0.66 (95%CI: 0.32, 1.35; I2 =0.0%, P =0.4333), with low heterogeneity and no publication bias.

4. Discuss

Biqi capsule is composed of ten traditional Chinese medicines including Strychnine, Codonopsis, salvia miltiorrhiza, Atractylodes atractylodes, Poria cocos, Ligusticum chuanxiong, Panax notoginseng, dithilong, licorice and Achyranthes bidentata. It can nourish qi and blood, dispel wind and dehumidize, promote blood circulation and relieve pain, treat deficiency of qi and blood, rheumatism block, muscle and joint pain, etc. It is mainly used in Chinese medicine "arthralgia" disease, and its curative effect has been widely recognized after years of clinical application. Modern pharmacological studies have shown that Biqi capsule has anti-inflammatory, detumescent and analgesic effects [12].

After treating AS with Biqi capsule, the effective rate was significantly improved compared with the control group, and the activity and function of AS were significantly improved. However, there was no significant difference between Biqi capsule and the control group in alleviating inflammation and the occurrence of adverse reactions.

Acknowledgments

Foundation Item: Key RESEARCH and Development Project of Science and Technology

ISSN 2706-6819 Vol.4, Issue 8: 72-78, DOI: 10.25236/IJFM.2022.040812

Department of Shaanxi Province, No.2021SF419; Key Research And Development Program of Social Development of Xianyang Science and Technology Bureau, No.2020K02-109; Discipline Construction Innovation Team of Shaanxi University of Traditional Chinese Medicine 2019YL-02); Study on the mechanism of acupotomy for femoral head necrosis

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ISSN 2706-6819 Vol.4, Issue 8: 72-78, DOI: 10.25236/IJFM.2022.040812

Table 1: Basic information table

In the literature	Published year	Male/female（N/C）	Course of disease (years)	Age（N）	Age（C）	methods	N/C	Period of treatment	Treatment group intervention measures	Control group intervention	Outcome indicators
RenYan	2022	50/20 52/18	3.82±1.15/3.97±1.21	32.93±8.21	33.15±8.30	random	70/70	12weeks	Biqi capsule 1.2g/ time TID+ control group	Tripterygium wilfordii glycosides 20mg/ TID	①
WangTao	2021	35/25 33/27	3.76±0.83/3.72±0.81	49.27±5.72	49.52±6.18	Envelope lottery	60/60	12weeks	Biqi capsule 1.2g/ time TID+ control group	Etanercept injection 25mg/ (kg·d) twice a week	①②③④⑤⑥
WangGuizhen	2020	52/8 53/7	8.08±5.56/8.52±4.91	31.48±8.32	31.31±8.36	Random number table method	60/60	12weeks	Biqi capsule 1.2g/ time TID	Sulfasalazine tablets, 4 tablets per BID	①②③④⑤⑥
LiuShenyi	2016	21/9 23/7	/	37.9±2.3	36.3±2.2	random	30/30	4weeks	Biqi capsule 1.2g/ time TID+ control group	Nonsteroidal anti-inflammatory and analgesic drugs + sulfasalazine	①②③
HeRonglong	2015	12/9 11/10	5.4±3.7/5.9±3.8	24.8±9.1	25.3±8.9	Random throw method	21/21	12weeks	Biqi capsule 1.2g/ time TID+ control group	Meloxicam + sulfasalazine 1g/ BID	①④⑤⑥
FuQiang	2014	14/6 16/4	4±3/4±4	25±4	24±5	Along with the machine	20/20	12weeks	Biqi capsule 1.2g/ time TID+ control group	Tripterygium wilfordii Moss tablets 20mg/ time TID+ Meloxicam dispersive tablets 7.5mg/ time BID	①②③④⑤⑥
WangXiaojing	2012	27/3 26/4	4±3/5±4	23±4	24±4	Along with the machine	30/30	12weeks	Biqi capsule 1.2g/ time TID+ control group	Meloxicam 7.5mg/ BID+ sulfasalazine 1.0g/ BID	①④⑤⑥

① Effective rate ②BASDAI score ③BASFI score ④CRP ⑤ESR ⑥ adverse reactions