

A Meta-analysis of Therapeutic Effect of Thalidomide on Ankylosing Spondylitis

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ABSTRACT

Objective: To study the therapeutic effect of thalidomide on ankylosing spondylitis (AS) by meta-analysis. **Methods:** Personal digital library, Cochrane library, and China Biology Medicine disc (CMBdisc), as well as relevant pharmaceutical and medical journals, were collected and reviewed. After the analysis of characteristics of the selected document and the evaluation of the risk of bias, the therapeutic effect of thalidomide on ankylosing spondylitis (AS) and its influence on related indexes were analyzed by literature data. **Results:** The meta-analysis results of 8 pieces of literature showed that the total effective rate of thalidomide in the treatment of ankylosing spondylitis (AS) was significantly improved, compared with conventional treatment or sulfasalazine (SASP) treatment ($P < 0.05$). Furthermore, the time of morning stiffness, BASDAI score, C-reactive protein (CRP) level, and other related symptoms and indexes were significantly optimized ($P < 0.05$). **Conclusion:** By rational utilization of thalidomide in the treatment of ankylosing spondylitis (AS), related symptoms and indexes of patients can be effectively improved, the total effective rate of the treatment was significantly improved and the safety of the treatment can be guaranteed.

1. Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease, spinal apophysis, sacroiliac joint, paraspinal soft-tissue and peripheral joint of patients will be invaded after onset. Moreover, extra-articular manifestations may also occur. The patients with more severe ankylosing spondylitis (AS) have the spinal deformity and ankylosis. At present, there is no radical cure for ankylosing spondylitis (AS) in clinical practice. Drug treatment, surgical treatment, and proper exercises are usually used to

relieve and control the disease. With the development and progress of drug research in recent years, the application of tumor necrosis factor- α (TNF- α) antagonist in clinical treatment is more and more extensive. This kind of medicine can not only quickly relieve the stiffness, pain, and other symptoms of patients but also inhibit bone destruction and improve body function and quality of life of the patients. However, due to the higher economic cost and the exclusion from urban medical insurance, such biological agents cannot be widely used in the clinical treatment of anky-

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losing spondylitis (AS). Related research and experiment of thalidomide (Thalomid) found that thalidomide can not only inhibit the production of TNF- α selectively by normal monocytes but also reduce the level of serum TNF- α of the patients with erythema nodosum leprosy (ENL) and tuberculosis (TB). Moreover, the application of thalidomide in the treatment of ankylosing spondylitis (AS) can obtain a relatively remarkable effect, and the related research is gradually enriched.

2. Materials and Methods

2.1 Inclusion Criteria

(1) Test type: contrast test.

(2) Type of patients into groups: diagnosed as ankylosing spondylitis (AS) without joint deformity.

(3) Test method: the control group was treated with conventional non-steroidal anti-inflammatory drugs (NSAIDs) or sulfasalazine (SASP), while the observation group was treated with thalidomide based on conventional treatment.

(4) Observation index: the total effective rate, morning stiffness time, finger to floor distance, occipital wall distance, Schober test, degree of chest expanding, BASDAI score, C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), number of peripheral joints with swelling and adverse reactions.

2.2 Retrieval Methods

Electronic retrieval was mainly used for data retrieval. Ankylosing spondylitis (AS) and thalidomide were input as keywords in the personal digital library, Cochrane library, and China Biology Medicine disc (CMBdisc) for literature search.

2.3 Data Filtering and Extraction

The first was to screen preliminarily the title and abstract of articles, and the second was to read the content of the articles to finally select the included literature.

2.4 Assessment of Risk of Bias

The Cochrane evaluation system was used to evaluate the risk of bias of the selected literature. The risk of bias of the selected literature was set as a, B and C, and the corresponding literature risk coefficient was low, medium, and high.

3. Results

3.1 Analysis Results of Literature Search

74 pieces of literature were initially collected through the

database search, and there were 38 left after screening. The literature with incomplete data and insufficient follow-up time were removed after full-text reading. Finally, 8 pieces of literature were selected as reference documents for the study, involving 610 patients with ankylosing spondylitis (AS). The reference documents are in Chinese or English.

3.2 Characteristics of Inclusion Documents and Analysis of the Risk of Bias

The eight reference documents included were all used for the study of the contrast test. The observation group was treated with thalidomide and the control group was treated with conventional treatment or sulfasalazine (SASP). The risk of bias of six reference documents was moderate, and that of two of them were low.

Table 1. Characteristics and Risk of Bias of Inclusion Documents (n = 8, $\bar{x} \pm s$)

Researcher (Year)	Study design	Number of patients		Assessment of risk of bias						
		T	NT	1	2	3	4	5	6	Grade
XIE Denghua (2020)	CT	40	40	Y	U	U	Y	Y	Y	B
WANG Zhe, ZHAO Xiaoying, QUAN Bingtao, et al. (2019)	CT	40	40	Y	U	U	Y	Y	Y	B
RAN Jian (2019)	CT	38	38	Y	U	U	Y	Y	Y	A
HOU Tao (2018)	CT	44	44	Y	U	U	Y	Y	Y	B
ZENG Xianlin (2017)	CT	32	32	Y	U	U	Y	Y	Y	B
GUI Yinli, SHI Lipu, XUN Wen, et al. (2017)	CT	41	41	Y	U	U	Y	Y	Y	B
LI Guangke & YUAN Yao (2016)	CT	30	30	Y	U	U	Y	Y	Y	A
LI Yonghong, TAO Li-hong & QIAN Kewei (2016)	CT	40	40	Y	U	U	Y	Y	Y	B

CT: contrast test; T: thalidomide; NT: non-thalidomide treatment; 1: random method; 2: randomly hidden; 3: blind method; 4: loss to follow-up; 5: selective reporting; 6: confounding bias; Y: appropriate; U: unclear; N: inappropriate

3.3 Statistical Analysis

Through a comprehensive analysis of relevant research results, thalidomide in the treatment of ankylosing spondylitis (AS) has a very significant therapeutic effect, improving the total effective rate of clinical treatment, and related indicators of patients.

3.3.1 The Total Effective Rate of Treatment

Six pieces of literature have studied the total effective rate of treatment. It was found by contrast test that the total clinical effective rate of thalidomide in the treatment of

ankylosing spondylitis (AS) is significantly higher than that of the conventional treatment or sulfasalazine (SASP) treatment.

3.3.2 Morning Stiffness Time

Four pieces of literature have studied the morning stiffness time. It was found by contrast test that the morning stiffness time of the patients in the observation group after treatment was significantly less than that of the patients in the control group and thalidomide could improve morning stiffness of the patients significantly.

3.3.3 Finger to Floor Distance and Occipital Wall Distance

One piece of literature has studied finger to floor distance and six pieces of literature have studied the analysis of occipital wall distance index. It was found by contrastive analysis that finger to floor distance and occipital wall distance of the patients after treatment all significantly declined but the two indexes of the patients after the treatment with thalidomide were lower than that of the patients in the control group.

3.3.4 The Number of Peripheral Joints with Swelling

Six pieces of literature have studied the number of peripheral joints with swelling. It was found by the study and tests that the number of peripheral joints with swelling of the patients after the targeted treatment significantly declined and the index of the observation group was significantly lower than that of the control group.

3.3.5 Schober Test

Two pieces of literature have studied the Schober test. It was found by contrast test that the Schober test result of the patients in the observation group after treatment was significantly higher than that of the patients in the control group and the difference between the two groups was statistically significant.

3.3.6 Degree of Chest Expanding

Eight pieces of literature have studied the degree of chest expansion. It was found by contrastive analysis that the degree of chest expansion of the patients in the observation group was significantly higher than that of the patients in the control group.

3.3.7 BASDAI Score

Three pieces of literature have studied the BASDAI score.

The score of the observation group after treatment was lower than that of the control group.

3.3.8 C-Reactive Protein (CRP) Level

Six pieces of literature have studied the C-reactive protein (CRP) level. The study found that the CRP level of the patients in the two groups after treatment significantly declined and the CRP level of the patients in the observation group was significantly lower than that of the control group.

3.3.9 Erythrocyte Sedimentation Rate (ESR)

Five pieces of literature have studied the erythrocyte sedimentation rate (ESR). Through comparison, we found that the ESR of the patients in the two groups after treatment significantly declined, and the ESR of the patients in the observation group was significantly lower than that of the patients in the control group.

3.3.10 Adverse Reactions

Three pieces of literature have studied adverse reactions. Some studies found that the incidence of adverse reactions of the patients treated with thalidomide was significantly lower than that of the patients treated with sulfasalazine (SASP), and sulfasalazine was more likely to cause skin dryness, drowsiness, and gastrointestinal reactions. Furthermore, other studies found that there was no difference in the incidence of dizziness, nausea, and vomiting between patients.

4. Discussions

Ankylosing spondylitis (AS) as a chronic inflammatory disease, may seriously affect the joint function and daily life of patients, causing damage to the physical and mental health, leading to lower quality of life of patients, and also causing greater pressure on patients' families and society. The traditional treatment of ankylosing spondylitis (AS) includes proper exercises and taking NSAIDs and SASP. In clinical treatment, the local glucocorticoid treatment is used. Tumor necrosis factor- α (TNF- α) antagonist has obvious effects in the treatment of ankylosing spondylitis (AS) but cannot be popularized and applied due to the high price. Thalidomide is a synthetic glutamic acid derivative, initially used in the treatment of pregnant women with pregnancy reaction, but limited due to neurotoxicity and teratogenesis. With the development and improvement of drug research, thalidomide has been gradually found and confirmed in inhibiting the production of TNF- α by monocytes, costimulation of human T lymphocytes, and assisting T-cell response, and

its clinical application is gradually extensive. In recent years, some studies have pointed out that thalidomide has more significant effects in the treatment of ankylosing spondylitis (AS), and has significant anti-inflammatory and anti-immune effects through its inhibition of angiogenesis and adhesion molecule activity. Animal experiments have confirmed the effect of thalidomide on the improvement of arthritis in rats.

In this study, The meta-analysis results of 8 pieces of literature showed that the total effective rate of thalidomide in the treatment of ankylosing spondylitis (AS) was significantly improved, compared with conventional treatment or sulfasalazine (SASP) treatment ($P<0.05$). Furthermore, the time of morning stiffness, BASDAI score, C-reactive protein (CRP) level, and other related symptoms and indexes were significantly optimized ($P<0.05$). Besides, thalidomide in the treatment of ankylosing spondylitis (AS) significantly improved the clinical symptoms of patients, promoted the recovery of joint function, and improved the quality of life of the patients. Meanwhile, thalidomide in the treatment of ankylosing spondylitis (AS) can play a significant role in immunosuppression and regulation, to form a good anti-inflammatory effect by targeting inhibition of neutrophil chemotaxis. In clinical treatment, a large number of studies and tests have confirmed the therapeutic effect of thalidomide in the treatment of ankylosing spondylitis (AS) and its significant effects on the improvement of disease-related indexes. Thoracic mobility of patients can reflect the severity of thoracic spine involvement. When thalidomide was applied in the treatment of ankylosing spondylitis (AS), the index of thoracic spine involvement of patients was significantly improved, and the severity of thoracic spine involvement was significantly reduced compared with the conventional treatment. Meanwhile, the results of the Schober test reflected the degree of lumbar spine involvement, and this index was significantly improved, indicating that the degree of lumbar spine involvement was significantly declined. Occipital wall distance reflected the degree of cervical spine involvement, and this index value declined, indicating the degree of cervical spine involvement declined. The time of morning stiffness shortened, indicating that the degree of peripheral joint involvement was significantly declined. All in all, thalidomide can significantly improve the symptoms of patients with ankylosing spondylitis (AS).

In conclusion, relevant symptoms and indexes of

patients can be effectively improved by the rational application of thalidomide in the treatment of ankylosing spondylitis (AS), the total effective rate of treatment significantly improved, and the safety of treatment can be guaranteed. Eight pieces of literature selected in the study for meta-analysis, the study is more dependent on the original data and has some limitations on the integrity and effectiveness of data information. Therefore, the conclusion of the study should be analyzed reasonably and used cautiously.

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