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A Meta-Analysis of Danhong Injection in the Treatment of Vascular Dementia

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Abstract

Objectives: To evaluate the efficacy of Danhong injection in the treatment of vascular dementia. Methods: CNKI, VIP, CBM, MEDLINE, PubMed, and SCI Expanded databases were searched, and the clinical research literature of Danhong injection in the treatment of vascular dementia was collected. Literature screening and literature quality assessment were performed independently by two investigators based on inclusion criteria and the Cochrane System Evaluator's Handbook version 5.0.0. Meta-analysis was performed using RevMan 5.0 software. Results: A total of 16 studies were included in a total of 1383 patients. Meta-analysis showed that Danhong injection combined with conventional chemotherapy can reduce the incidence of vascular dementia compared with conventional chemotherapy alone (odds ratio 3.13, 95% CI2.02 to 4.85, P < 0.0001), improved Mini-mental State Examination (MMSE)) score (SDD 1.76, 95% CI 0.67 to 2.85, P = 0.002). Conclusion: Danhong transfusion combined with chemical drugs for the treatment of vascular dementia is superior to the simple treatment of chemical drugs, which can improve the efficacy and quality of life of patients, indicating that Danhong injection has an auxiliary effect on the treatment of vascular dementia.

Keywords

Danhong Injection, Vascular Dementia, Meta-Analysis

1. Introduction

Vascular dementia (VD) is an acquired intellectual impairment syndrome caused by brain dysfunction caused by various cerebrovascular diseases. In addition to the symptoms and signs of neurological localization damage, there are a series of abnormal neuropsychological symptoms and mental behaviors. With the increase of the proportion of aging population in China, the prevalence of VD is

significantly higher than before. It is currently the second leading cause of Alzheimer's disease, second only to Alzheimer's disease [1]. The type of disease seriously threatens the quality of life of patients and adds a heavy load to the family, society and the country. As a progressive disease, VD has a poor prognosis, and there is no ideal therapeutic drug. Clinically, it mainly provides treatments such as improving cerebral circulation and reviving brain metabolism [2].

Danhong injection is a compound preparation made of Chinese herbal medicine *Salvia miltiorrhiza* and safflower extract. *Salvia miltiorrhiza* contains active ingredients such as salvianolic acid and tanshinone. Salvianolic acid can increase adenosine triphosphate (ATP) content, increase mitochondrial potential, inhibit cytochrome release, inhibit the expression of apoptotic factors up-regulated by apoptosis, and inhibit neuronal apoptosis. The other component of safflower can inhibit platelet adhesion and aggregation, improve the balance of vasospasm and vasoconstrictor, and protect brain microvascular endothelial cells. There are also clinical studies showing that Danhong injection can improve brain microcirculation, protect brain tissue in the penumbra of ischemic area, and improve neurological dysfunction [3]. However, in the existing clinical trials, most of the randomized controlled trials are spontaneous small-scale clinical trials, which cannot comprehensively and systematically analyze the effect of Danhong injection on VD. This study used a systematic review method to search the published randomized controlled trial of Danhong injection in the treatment of vascular dementia for meta-analysis.

2. Methods

2.1. Inclusion Criteria

Studies were considered to be eligible for inclusion if they met all of the following criteria: 1) The study design is randomized controlled trials (RCTs), whether blinded or not. Exclude documents with incomplete data, incorrect data, and repeated publications; 2) The type of patient is not limited. All cases met the Chinese Medicine Association Neurology Branch "Diagnostic Criteria for Vascular Dementia", the "Guidelines for Clinical Research of New Drugs for the Treatment of Dementia" issued by the Ministry of Health, or the American Neurological Society's Handbook of Diagnostics and Statistics for Neuropathy. Diagnostic criteria for vascular dementia; 3) The experimental group was treated with Danhong injection combined with conventional chemotherapy. The control group received conventional chemotherapy, including aspirin, sibutramine, nimodipine, oxiracetam, butylphthalide, and vasodilators, energy mixture, vitamins, etc; 4) The outcome criteria for outcomes are expected to be clear, including at least one of the following outcome measures: the effectiveness of treatment, the score of the Simple Intelligent Mental State Energy Meter (MMSE), and the score for activities of daily living (ADL).

2.2. Search Strategy

Comprehensive literature searches were conducted in CNKI Database, Chinese

biomedical Literature Database, VIP database, Medline, PubMed, SCI Expanded. The search time was built for each database until December 31, 2018. The English search terms are: vascular dementia, Danhong. Chinese search terms are: Xueguanxingchidai, Danhong. Manually retrieve relevant materials and bibliography of each paper.

2.3. Data Screening and Literature Quality Evaluation

First, two research members independently read all the literature titles and abstracts to determine whether they meet the inclusion criteria. The documents that are not included in the uncertainty should be read and then judged; then, cross-check the test results. If there is any disagreement, it will be resolved through discussion between the two parties. If there are still differences, the third person will judge it. The extraction of the literature is implicit in the quality assessment of the Cochrane System Evaluator's Manual (including whether the resulting data is complete, randomized, whether blinded, etc.)

2.4. Statistical Analysis

Statistical analysis was performed using Revman 5.3. When the statistical data is a two-category variable, the relative risk (RR) and the 95% confidence interval (95% CI) was the effect analysis statistic. When the analysis index was continuous variable, the mean difference (MD) and 95% CI were used as the efficacy statistic.

Heterogeneity test: Chi-square test. When ($P > 0.10$, $I2 < 50\%$), there was no statistical heterogeneity, and the fixed effect model was used for meta-analysis; when ($P < 0.10$, $I2 > 50\%$), there was statistical heterogeneity, if not For clinical heterogeneity or methodological heterogeneity, a random effect model was used for meta-analysis; if clinical heterogeneity was present, a chi-square test was used. When ($P > 0.10$, $I2 < 50\%$), there was no statistical heterogeneity 2, and a fixed effect model was used for meta-analysis; when ($P < 0.10$, $I2 > 50\%$), there was statistical heterogeneity. If there is no significant clinical heterogeneity or methodological heterogeneity, a random effects model is used for meta-analysis; when clinical heterogeneity exists, sensitivity analysis or subgroup analysis is performed based on its source. If the heterogeneity is too large to abandon the meta-analysis, a descriptive analysis is used.

3. Results

3.1. Basic Characteristics of the Included Literature

At the beginning, 38 articles were first retrieved, including 38 Chinese databases and 0 English databases. After screening by the researchers, 16 studies [4]-[19] were included, which were all published in Chinese, with a total of 1383 cases. Twelve of the studies [6] [7] [8] [9] [11]-[16] [19] took efficient as outcome. Eleven of the studies [1]-[6] [10] [12] [13] [14] [16] [17] [18] took MMSE score as outcome. The basic characteristics of the included studies are shown in **Table 1**.

Table 1. Basic characteristics of inclusion in the study.

Author	Number		Interventions		Duration	Outcome
	Experimental	Control	Experimental	Control		
Wu 2017 [4]	52	52	Danhong injection + chemistry medicine	Chemistry medicine	120d	②
Jin 2008 [5]	55	53	Danhong injection + chemistry medicine	Chemistry medicine	28d	②
Jin 2010 [6]	42	38	Danhong injection + chemistry medicine	Chemistry medicine	28d	① ②
Zhang 2010 [7]	25	25	Danhong injection + chemistry medicine	Chemistry medicine	28d	①
Qin 2009 [8]	36	32	Danhong injection + chemistry medicine	Chemistry medicine	30d	① ②
Deng 2010 [9]	40	40	Danhong injection + chemistry medicine	Chemistry medicine	50d	①
Jin 2010 [10]	40	40	Danhong injection + chemistry medicine	Chemistry medicine	28d	②
Guo 2009 [11]	42	38	Danhong injection + chemistry medicine	Chemistry medicine	28d	①
Wang 2013 [12]	45	45	Danhong injection + chemistry medicine	Chemistry medicine	126d	① ②
Wang 2017 [13]	56	56	Danhong injection + chemistry medicine	Chemistry medicine	84d	① ②
Liu 2012 [14]	35	35	Danhong injection + chemistry medicine	Chemistry medicine	56d	① ②
Liu 2015 [15]	64	64	Danhong injection + chemistry medicine	Chemistry medicine	84d	①
Shi 2011 [16]	40	43	Danhong injection + chemistry medicine	Chemistry medicine	28d	① ②
Wang 2011 [17]	40	42	Danhong injection + chemistry medicine	Chemistry medicine	50d	②
Yuan 2010 [18]	34	30	Danhong injection + chemistry medicine	Chemistry medicine	28d	②
Zhao 2016 [19]	52	52	Danhong injection + chemistry medicine	Chemistry medicine	28d	①

①Efficient ②MMSE.

3.2. Quality Evaluation

Of the included studies, only four studies described the use of random number table grouping, and the remaining 12 studies were not specified in the randomized protocol. None of the studies reported hidden allocation. All studies did not report whether blinding was used. None of the patients were lost to follow-up in all trials and no patients were withdrawn. The bias analysis of the included studies is shown in Figure 1.

3.3. Efficient Comparison

Seven studies reported the effectiveness of a total of 583 patients, of which 299 patients were treated with Danhong injection combined with conventional chemotherapy, and 284 patients were treated with conventional chemotherapy alone. There was no heterogeneity between the groups (P = 0.99, I2 = 0%), and the fixed effect model was used for Meta analysis. Figure 2 shows that compared with conventional chemotherapy alone, Danhong injection combined with chemical drugs was more effective in the treatment of vascular dementia. The effective rate of the two groups was statistically significant (OR = 3.13, 95% CI [2.02, 4.85], P < 0.0001).

3.4. Mini-Mental State Examination (MMSE) Score

Twelve studies reported MMSE scores. There were 1116 patients, of which 566

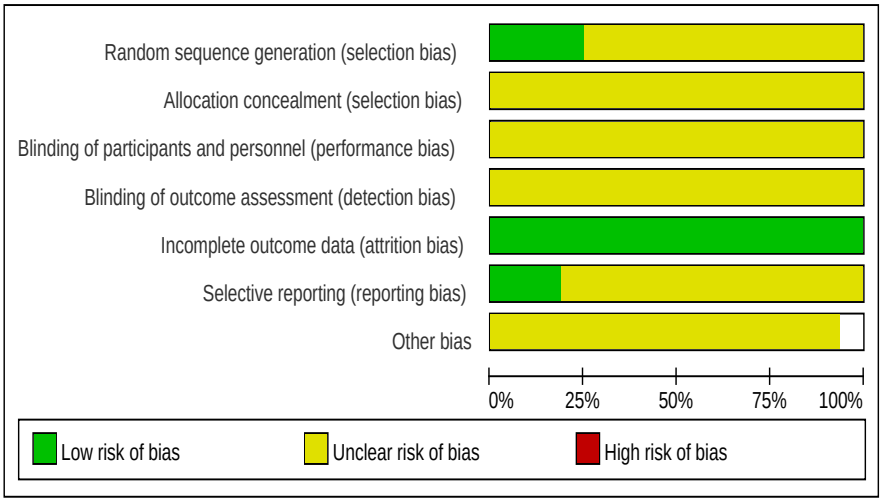

Figure 1. Risk of bias assessment.

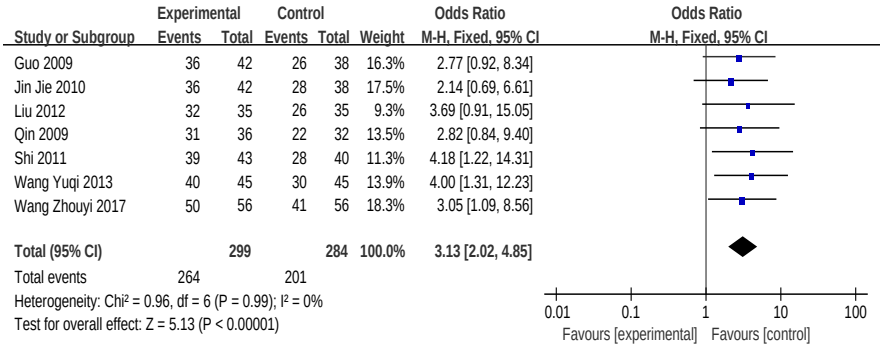

Figure 2. Meta-analysis of the effectiveness of Danhong injection in the treatment of vascular dementia.

were treated with Danhong injection combined with conventional chemotherapy, and 550 patients were treated with conventional chemotherapy. There were heterogeneity differences among the components ($P < 0.00001$, $I2 = 87\%$), but the source of the difference is unknown, and subgroup analysis is not possible, so the random effect model is used for meta-analysis. **Figure 3** shows that the MMSE scores of Danhong injection combined with conventional chemotherapy were higher than those of conventional chemotherapy alone, and the two were statistically different (SDD = 1.76, 95% CI [0.67, 2.85], $P = 0.002$).

3.5. Publication Bias

Publication bias was used to perform a funnel plot analysis of the included studies. **Figure 4** showed that the included studies were asymmetrically distributed, suggesting that there may be publication bias.

4. Discussion

Danhong injection is a compound preparation made from Chinese herbal medicine *Salvia miltiorrhiza* and safflower extract, which is only used in China. The

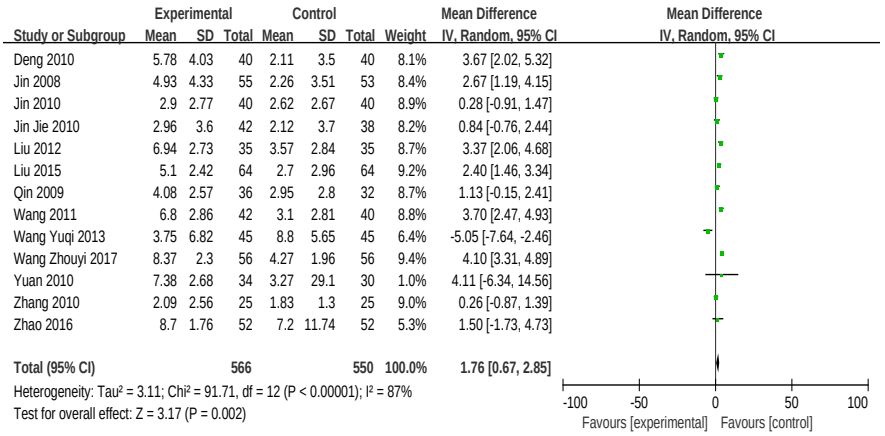

Figure 3. Meta-analysis of Danhong injection in the treatment of vascular dementia with MMSE score.

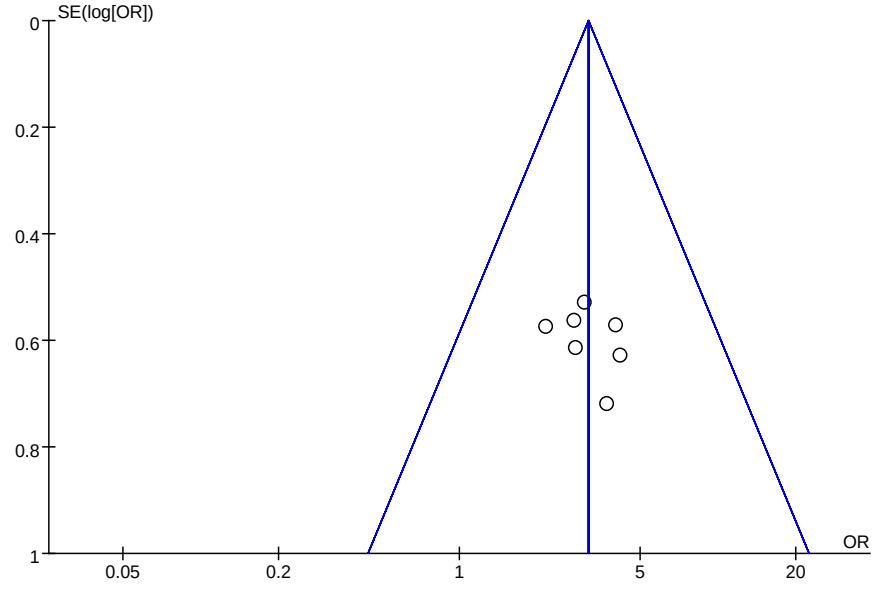

Figure 4. Funnel diagram of effective treatment of vascular dementia with Danhong injection.

included studies are also published in domestic journals on the clinical trial of Danhong injection for the treatment of VD. Compared with the conventional treatment with chemical drugs alone, Danhong injection combined with conventional chemotherapy can improve the efficiency, improve the mental state of mind, and improve the life treatment of patients.

However, this study also has certain limitations. First, the quality of the included literature is low. The included trials rarely describe random grouping methods and hidden assignments. The description of the intervention is also lacking in specificity. Second, because the number of documents included in this study is small, and the sample size of the study is small, the test efficiency is low.

At the same time, when we analyzed the MMSE scores, the heterogeneity among the included studies was large, which may be related to the subjective er-

rors caused by different types of chemical drugs used in the interventions, different doses, different treatment courses and the scores of the researchers. However, the literature does not provide a detailed description of the scoring.

5. Summary

In summary, Danhong injection combined with chemical drugs for the treatment of vascular dementia is better than the conventional chemotherapy treatment, indicating that Danhong, this infusion has a certain auxiliary effect on the treatment of vascular dementia. However, the number of studies included in this study is small, the sample size is small, and the quality is not high, which may lead to a certain bias in the evaluation conclusions of this system. Therefore, it is still necessary to further develop large-sample, multi-center, random doubles with unified outcome indicators, blind controlled trial to further validate the efficacy and safety of the injection in patients with VD.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Ding, J. (2013) Risk Factors of Vascular Dementia and Clinical Analysis of Comprehensive Diagnosis and Treatment. *China Medical Science*, No. 20, 178-179.

[2] Li, Q., Yan, X.C., Nie, J.T. and Yu, W.T. (2018) A Survey of Traditional Chinese Medicine in the Treatment of Vascular Dementia. *Clinical Research of Traditional Chinese Medicine*, **10**, 32-36.

[3] Ren, P., Zhou, M.X., Liu, W.H. and Liu, H.X. (2016) Progress in the Pharmacological Effects of Danhong Injection in the Treatment of Cardiovascular and Cerebrovascular Diseases. *Progress in Modern Biomedicine*, No. 31, 6197-6200.

[4] Wu, J. (2017) The Relationship between Donepezil and Danhong Injection in the Treatment of Cognitive Function and Nervous System in Elderly Patients with Vascular Dementia. *Medical Theory and Practice*, **30**, 3610-3612.

[5] Jin, J., Yu, H. and Chen, H. (2008) Therapeutic Effect of Danhong Injection on Vascular Dementia. *Journal of Medicine Forum*, **29**, 27-28+31.

[6] Jin, J., Yu, H. and Chen, H. (2010) Treatment of 40 Cases of Vascular Dementia with Danhong Injection. *Chinese Journal of Experimental Formulation*, **16**, 198-200.

[7] Li, Z., Hui, T., Wang, Y., Wang, H. and Yuan, L.J. (2010) efficacy of Vascular Dementia Danhong Injection. *Modern Journal of Medicine*, **19**, 788-789.

[8] Qin, F. and Liu, X. (2009) Clinical Observation of 68 Cases of Vascular Dementia Treated with Danhong Injection. *Modern Chinese Medicine Application*, **3**, 141-142.

[9] Deng, Y. (2010) A Comparative Study of 40 Cases of Vascular Dementia Treated with Danhong Injection. *Journal of Practical Cardiopulmonary and Pulmonary Diseases*, **18**, 322-323.

[10] Jin, J., Jia, J. and Guo, Z. (2010) Clinical Study of Danhong Injection in the Treat-

ment of Vascular Dementia and Its Effect on β-Ap and Apo B. *Journal of Traditional Chinese Medicine*, **25**, 271-273.

[11] Guo, Z., Jin, J. and Jia, J. (2009) Treatment of 42 Cases of Qi Stagnation and Blood Stasis Type Vascular Dementia with Danhong Injection. *Chinese Journal of Practical Nervous Diseases*, **12**, 59-61.

[12] Wang, Y. (2013) Clinical Observation of Danhong Injection Combined with Nimodipine in the Treatment of Vascular Dementia. *Chinese Community Physician* (*Medical*), **15**, 209.

[13] Wang, Z., Huang, H., Xiao, Z., Chen, H. and Xia, G. (2017) Clinical Efficacy of Danhong Injection Combined with Nimodipine in the Treatment of Vascular Dementia and Its Effects on Serum VEGF, E2, Livin and β-Ap. *Chengdu University of Traditional Chinese Medicine Journal*, **40**, 53-55.

[14] Liu, G. (2012) Danhong Injection Combined with Nimodipine in the Treatment of 35 Cases of Vascular Dementia. *Chinese Pharmaceutical Industry*, **21**, 105-106.

[15] Liu, W. (2015) Clinical Efficacy of Danhong Injection Combined with Donepezil in the Treatment of Vascular Dementia and Improvement of Patients' Quality of Life. *Strait Pharmaceutical*, **27**, 162-163.

[16] Hai, S., Zhang, H., Zhao, M.Y., *et al*. (2011) Danhong Injection Combined with Piracetam. *Clinical Medical Journal*, **39**, 43-45.

[17] Wang, R. (2011) Therapeutic Effect of Danhong Injection on 42 Patients with Vascular Dementia. *Modern Preventive Medicine*, **38**, 2203-2204.

[18] Yuan, Q. (2010) Therapeutic Effect of Danhong Injection on Cognitive Impairment of Vascular Dementia. *Journal of Practical Cardiopulmonary and Pulmonary Diseases*, **18**, 1088-1089.

[19] Zhao, H., Zhao, Y. and Cai, F. (2016) Clinical Study of Danhong Combined with Butylphthalide in the Treatment of Vascular Cognitive Impairment. *Chinese Journal of Traditional Chinese Medicine*, **34**, 975-977.