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Meta-analysis of angelica Sini Decoction in the treatment of diabetic peripheral neuropathy

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Abstract: *[Objective] To systematically evaluate the effectiveness of Angelica Sini Decoction in the treatment of DPN.[Method] Randomized controlled trials of Angelica Sini Decoction in the treatment of DPN as of December 2020 were searched using RevMan 5.4.[Result] A total of 12 literatures and 936 patients were included. The total effective rate of experimental group was higher than that of control group [I^2=0%, RR=1.38,95%CI(1.28,1.48), P<0.00001], and further reduced TCSS score [I^2=44%, MD=1.43,95%CI(1.00,1.86),P<0.00001], improved peroneal sensation [I^2=0%, MD=3.59,95%CI (2.87,4.31), P<0.0001] and motor nerve conduction velocity [I^2=0%, MD=6.07, 95%CI(5.21,6.93), P<0.00001].[Conclusion] Angelica Sini Decoction is effective and safer in the treatment of DPN. Angelica Sini Decoction is better in improving the clinical efficiency of diabetic peripheral neuropathy, reducing TCSS score and improving peroneal nerve conduction velocity, with higher safety.*

Keywords: *Angelica Sini Decoction, DPN, Meta analysis*

1. Introduction

The prevalence of diabetic peripheral neuropathy (DPN) was as high as 51.1% in China in 2013[1], its clinical manifestations are diverse and insidious, with varying degrees of pain, numbness, cold, impotence and other symptoms. In severe cases, diabetic foot may occur, even amputation, which seriously affects the quality of life of patients. Although the name of DPN was not recorded in the ancient literature, the clinical manifestations of DPN were in the range of "dispersion-thirst paralysis, numbness, pain syndrome and flaccidity syndrome"[2]. Western medicine mainly to nutrition nerve, improve microcirculation, local pain and other symptomatic support therapy[3]. Chinese medicine believes that a variety of reasons lead to Yin Jin deficiency, blood stasis, Yin damage and inability of Yang Qi or Yang Qi can not reach the end of the limbs, DPN symptoms gradually appear. It was found that Angelica Sini Decoction in "Treatise on Febrile Diseases" can play a role by regulating NF-κb[4], RhoA/ROCK[5], Ca^{2+}, AGEs-RAGE[6-8] and other signaling pathways, or by reducing inflammatory factors[9] and improving the expression levels of TrkA protein[10]. The clinical data of Angelica Sini Decoction in the treatment of DPN were analyzed to provide more ideas for the treatment of DPN.

2. Data and methods

2.1 Inclusion criteria

①Randomized controlled trial(RCT), ②Meets the diagnostic criteria for DPN, ③The control group was treated with mecobalamin, and the experimental group was treated with Angelica Sini Decoction and its dosage, times of administration and course of treatment not limited, ④Underlying treatment remained consistent, ⑤The study indicators were total effective rate, TCSS score, and peroneal nerve conduction velocity.

2.2 Exclusion criteria

①Poor quality literatures, ②Combination with other traditional Chinese medicines.

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2.3 Search methods

RCTs of DPN treated by Angelica Sini Decoction and mecobalamin were retrieved from CNKI, VIP, Wanfang and Pubmed as of December 2020. The key words were Angelica Sini Decoction and Diabetic peripheral neuropathy.

2.4 Data extraction

By browsing the title, abstract and full text, identify the included literature and extract relevant information.

2.5 Quality assessment

Judgements regarding study design, data integrity and others[11] were made using the risk of bias assessment tool.

2.6 Statistical analysis

Analysis and processing was performed using RevMan5.4. Count data were expressed as relative risk(RR), and continuous variables were expressed as mean difference(MD). All were presented as means with 95% confidence interval(CI). Differences were considered statistically significant when $P \leq 0.05$. When $I^2 \leq 50\%$ indicated little heterogeneity, a fixed effects model was used. When $I^2 > 50\%$ indicated large heterogeneity, the random effects model was used. Funnel plots were plotted for the analysis of publication bias.

3. Result

Twelve RCTs[12-23] with 470 patients in the test group and 466 patients in the control group comprising 936 patients with DPN were finally included.

3.1 The screening flow is shown in Figure 1

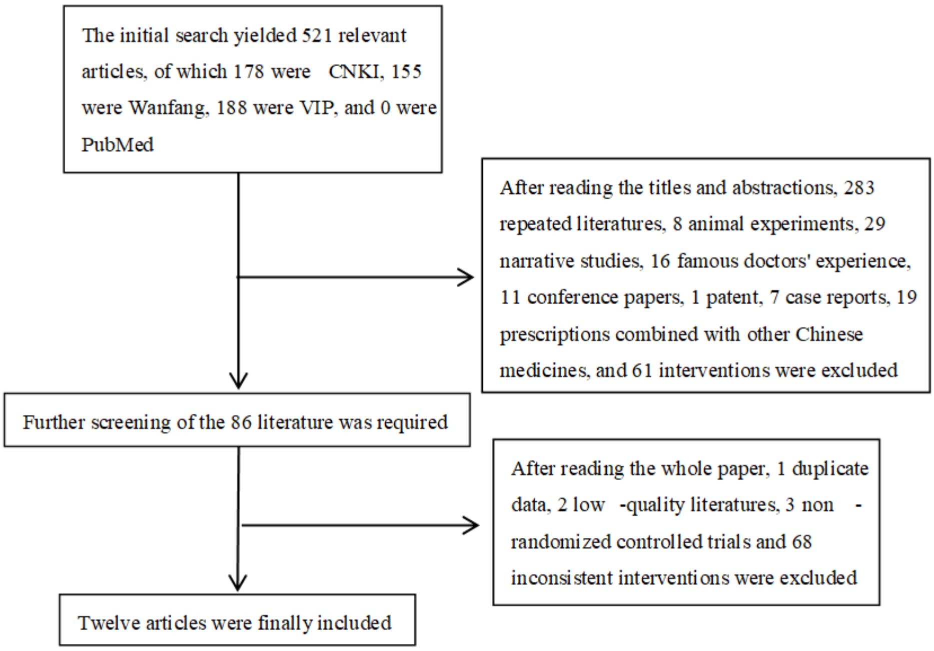

Figure 1

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3.2 Basic characteristics of the included literature are shown in Table 1, Quality evaluation is shown in Figure 2

Table 1

Included literature	The ratio of men to women(T, C)		age(T, C)		course of disease (T, C)		time	Basic treatment	study indicators	Principles of grouping
Yingxue Zhao etc[14]	30/20	28/22	64.58 ± 7.95	65.12 ± 8.21	12.21 ± 6.44	12.54 ± 6.41	4 W	Health Education, medication and dietary control	①②③	random
Kaiqiong Wei[16]	14/9	13/10	49.52 ± 9.44	49.65 ± 9.58	Not mentioned		4 W	Control of blood glucose, dietary control and exercise	①②③	Sequential treatment
Manya Wang[20]	15/15	17/13	53.27 ± 10.02	56.30 ± 8.57	3.97 ± 2.56	3.98 ± 2.37	4 W	Health Education and medication control	①	random
Haijun Wang[17]	24/13	23/14	57.6 ± 4.5	58.1 ± 4.2	8.4 ± 1.5	9.1 ± 1.2	4 W	medication and dietary control, exercise	①③	Randomization according to order of patient hospitalization
Wei Ding ect[15]	22/18	23/17	54.5 ± 8.3	53.6 ± 7.8	1~7	1~8	4 W	Control of blood glucose, dietary control and exercise	①②	random numbers table
Weini Chen ect[12]	15/15	17/13	61.40 ± 8.22	61.40 ± 7.04	8.45 ± 3.44	8.28 ± 1.92	4 W	medication and dietary control	②	random numbers table
Pengzhan Huang[18]	30/30	40/20	41~79	40~72	6~20	5~19	4 W	medication and dietary control, exercise	①	Differences in treatment methods
Chuangao Li[19]	30/20	28/22	41~79	40~80	6~19	5~20	4 W	medication and dietary control, exercise	①	random
Xianhua Zhang[13]	13/23	12/24	42~75	40~72	11.05 ± 3.78	10.25 ± 4.78	1 M	medication and dietary control	①	random
Jun Xue ect[23]	54*	51*	Not mentioned				8 W	Injection of insulin and Mecobalamin, dietary control and exercise	①②③	random numbers table
Feng Liu[21]	15/15	11/19	57.73 ± 6.17	55.29 ± 6.09	8.6 ± 1.52	82.4 ± 1.73	4 W	Health Education, medication and dietary control	①	random
Yanling Yang[22]	18/12	17/13	60.3 ± 9.58	61.6 ± 12.08	5.64 ± 4.77	5.49 ± 4.32	3 M	Health Education, medication and dietary control, exercise	①	random numbers table

Annotation: There was no significant difference in the general data among studies(P>0.05).In the test group, Angelica Sini Decoction was added and reduced, and the morning and evening were warmed. In the control group, Mecobalamin was administered three times a day.

*The male to female ratio was not mentioned.

①total effective rate, ②peroneal nerve conduction velocity, ③TCSS score.

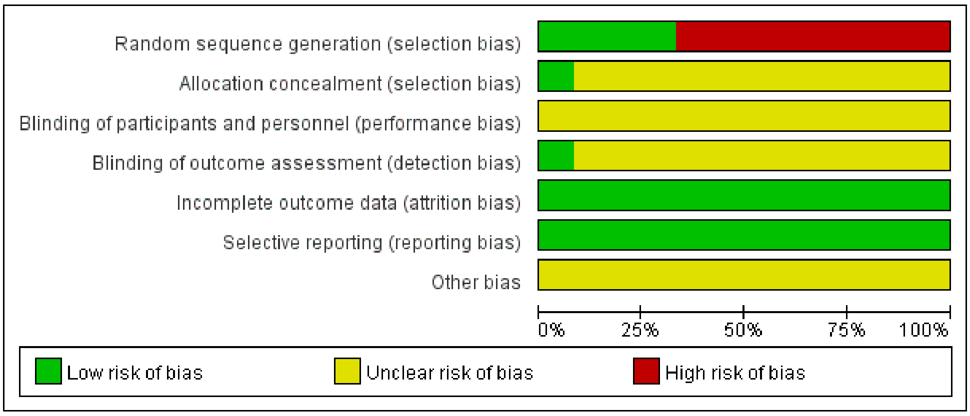

Figure 2

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3.3 Results of meta-analysis

3.3.1 The total effective rate

Eleven trials[13-22] were included and total effective rate was higher in the trial group than in the control group[I^2=0%, RR=1.38,95%CI(1.28,1.48), P<0.00001].

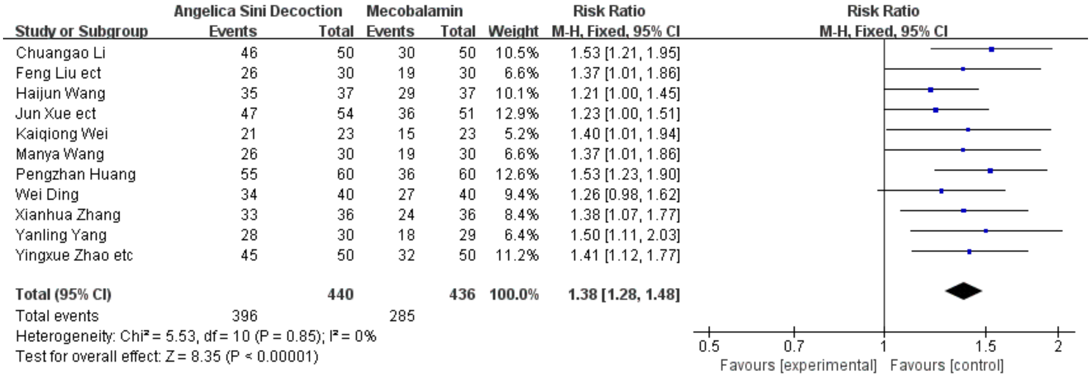

Figure 3

3.3.2 TCSS scores

Four trials[14,16,17,23] were included, with lower TCSS scores in the test group than in the control group[I^2=44%, MD=1.43,95%CI(1.00,1.86), P<0.00001].

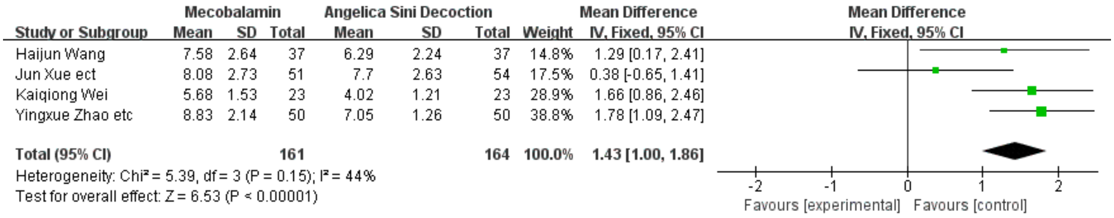

Figure 4

3.3.3 The common peroneal sensory nerve conduction velocity

Five trials[12,14-16,23] were included, in which the common peroneal sensory nerve conduction velocity of the common peroneal nerve might be higher in the test group than in the control group[I^2=95%, MD =5.55, 95%CI(2.40,8.59), P=0.0005].

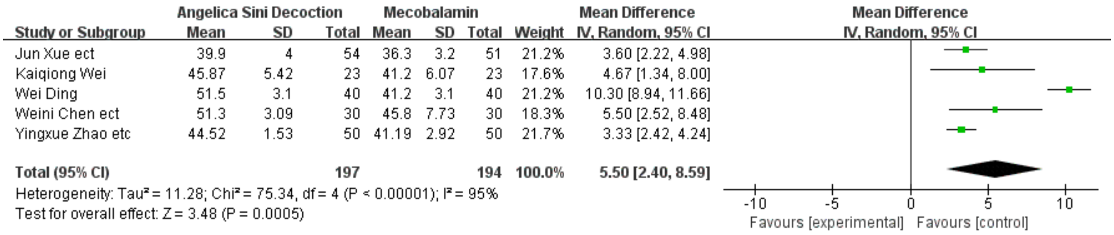

Figure 5

3.3.4 The common peroneal nerve motor nerve conduction velocity

Five trials[12,14-16,23] were included, in which the common peroneal nerve motor nerve conduction velocity of the test group might be higher than that of the control group[I^2=85%, MD=4.64, 95%CI(2.75,6.53), P<0.00001].

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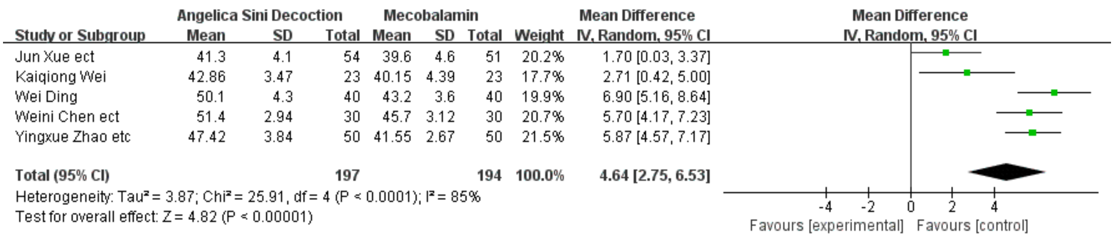

Figure 6

3.3.5 Sensitivity analysis

Table 2

After excluding clinical trials	I^2(%)	P	95%CI	
Random effect model	95	0.0005	2.40	8.59
Fixed effect model	95	<0.00001	4.43	5.70
Wei Ding ect[15]	0	<0.0001	2.87	4.31
Jun Xue ect[23]	96	0.005	1.82	10.16
Yingxue Zhao etc[14]	94	0.002	2.14	10.02
Weini Chen ect[12]	96	0.003	1.90	9.10
Kaiqiong Wei[16]	96	0.002	2.12	9.23

After excluding Wei Ding etc[15], we found that the sensory nerve conduction velocity of the common peroneal nerve was higher in the test group than in the control group[I^2 = 0%, MD = 3.59, 95%CI(2.87,4.31), P<0.0001].

Table 3

After excluding clinical trials	I^2(%)	P	95%CI	
Random effect model	85	<0.00001	2.75	6.53
Fixed effect model	85	<0.00001	4.18	5.63
Wei Ding ect[15]	85	0.0002	1.96	6.19
Jun Xue ect[23]	65	<0.00001	4.07	6.87
Yingxue Zhao etc[14]	87	0.0006	1.84	6.74
Weini Chen ect[12]	88	0.0005	1.91	6.78
Kaiqiong Wei[16]	86	<0.00001	2.96	7.15
Wei Ding ect[15],Jun Xue ect[23]	66	<0.00001	3.35	6.64
Wei Ding ect[15], Yingxue Zhao etc[14]	84	0.01	0.78	6.04
Wei Ding ect[15], Weini Chen ect[12]	88	0.02	0.65	6.32
Wei Ding ect[15], Kaiqiong Wei[16]	88	0.0005	1.93	6.99
Jun Xue ect[23], Yingxue Zhao etc[14]	76	<0.00001	3.08	7.38
Jun Xue ect[23], Weini Chen ect[12]	76	<0.00001	3.25	7.37
Jun Xue ect[23], Kaiqiong Wei[16]	0	<0.00001	5.21	6.93
Yingxue Zhao etc[14], Weini Chen ect[12]	90	0.03	0.43	7.14
Yingxue Zhao etc[14], Kaiqiong Wei[16]	90	0.002	1.75	7.78
Weini Chen ect[12], Kaiqiong Wei[16]	91	0.001	1.89	7.77

After excluding Kaiqiong Wei[16] and Jun Xue etc[23], we found that the motor nerve conduction velocity of the common peroneal nerve was higher in the test group than in the control group[I^2=0%, MD=6.07, 95%CI(5.21,6.93), P<0.00001].

The analysis of publication bias was performed with the total effective rate as the outcome measure, and the symmetry of inverted funnel plot was suboptimal, which indicated that there was publication bias, considering some factors related to the dosage of Angelica Sini Decoction, low quality of included literatures and insufficient sample size of clinical trials.

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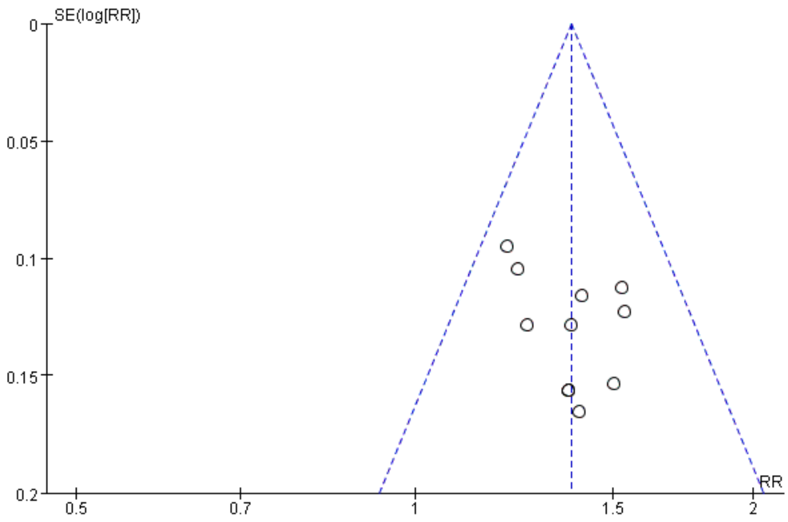

Figure 7

4. Discuss

A meta-analysis showed that Angelica Sini decoction was superior to Mecobalamin in improving the total effective rate, reducing TCSs score, and improving common peroneal nerve conduction velocity in diabetic peripheral neuropathy. However, the reliability of the results was reduced due to the increased risk of bias caused by the low number of included articles, low quality, variable study period and lack of follow-up. Angelica Sini Decoction footbath[24,25] also ameliorates symptoms associated with DPN, providing further evidence that Angelica Sini decoction has a significant effect on DPN. So more in-depth, high-quality, and larger scale clinical experimental studies are expected to validate the efficacy of Angelica Sini Decoction for DPN. At the same time, the evidence-based basis of safety evaluation of Danggui Si decoction was added.

References

[1] Zhu Wenbo, Kuang Hongyu. Research progress of diabetic peripheral neuropathy [J]. Journal of Cardiovascular Rehabilitation Medicine, 2020, (06): 736-739.

[2] Zhu Pu. Pang Guo-ming, chief physician, clinical treatment of diabetic peripheral neuropathy [A] // the first Chinese Traditional Chinese Medicine Diabetes Forum proceedings of China Diabetes Association 2019 [C]. Kaifeng, Henan, China: 209:3.

[3] Chinese guidelines for prevention and treatment of type 2 diabetes mellitus (2017 edition) [J]. Chinese Journal of Practical Internal Medicine, 2018, (04): 292-344.

[4] Cheng Siyu, Zhou Xiaojing, Li Xin, et al. Research on protective mechanism of Angelica Sini Decoction on diabetic peripheral neuropathy based on NF-κB signaling pathway [J]. Journal of Changchun University of Traditional Chinese Medicine, 2019, (01): 128-131.

[5] Xiang Qingwei. Effects of Angelica Sini Decoction on peripheral neuropathy and aquaporin 1, RhoA/ROCK signaling pathway in diabetic blood stasis rats [J]. Journal of Microcirculation, 2018, (03): 6-11.

[6] Xing Qichang, Chen Jia, Liu Zheng, et al. Prediction of target and mechanism of Angelica Sini Decoction for diabetic peripheral neuropathy [J]. Chinese Journal of Traditional Chinese Medicine Information, 2020,(06):101-105.

[7] Zhou Xiaojing, Li Jing, Yu Jiangbo, et al. Effects of Angelica Sini Decoction on diabetic peripheral neuropathy and glyoxalase ⅰ in rats [J]. Chinese Journal of Gerontology, 2018,(21): 532-5304.

[8] Zhou Xiaojing, Li Xin, Liu Yehui, et al. Effects of Angelica Sini Decoction on AGEs/RAGE and DPN in rats [J]. Chinese Journal of Gerontology, 2018,(22):5522-5524.

[9] Wu Meijuan, Du Fafei, Chen Yifei, et al. Effects of Angelica Sini Decoction on nerve conduction velocity and Levels of AEGs, CYS-C and Hcy in diabetic peripheral neuropathy [J]. World Science and Technology-Modernization of Traditional Chinese Medicine,2018,(09):1673-1678.

[10] Sun Jing. Effects of Angelica Sini Decoction combined with Mecobalamine on SNCV, MNCV, NGF and TrkA of sciatic nerve in diabetic peripheral neuropathy rats [D]. Dalian Medical University,2018.

ISSN 2618-1584 Vol. 3, Issue 5: 30-36, DOI: 10.25236/FMSR.2021.030505

[11] Liu Ming. System Evaluation, Meta-analysis design and Implementation Methods [M]. Beijing: People's Medical Publishing House, 2011.
[12] Chen Weini, Li Jun, Zhang Huang, et al. Effects of Angelica Sini Decoction on AEGs and its receptor in diabetic peripheral neuropathy [J]. Shanxi traditional Chinese medicine, 2016, 32(06): 12-14.
[13] Zhang Xianhua. Angelica Sini Decoction for the treatment of 36 cases of diabetic peripheral neuropathy [J]. Journal of shanxi university of traditional Chinese medicine, 2010,11(04):46-47.
[14] Zhao Yingxue, Liu Zhiyong, Dong Ning, et al. Application of Angelica Sini Decoction in diabetic peripheral neuropathy and its effect on electrophysiological level [J]. Chinese journal of traditional Chinese medicine, 2019, 37(11): 2748-2750.
[15] Ding Wei, Chen Wei, Li Jing. Journal of Liaoning university of traditional Chinese medicine, 2016, 18(09): 123-125. (in Chinese)
[16] Wei kaiqiong. Clinical value of Angelica Sini Decoction in the treatment of diabetic peripheral neuropathy [J]. Psychological monthly, 2019, 14(12): 186.
[17] Wang Haijun. Clinical observation of Angelica Sini Decoction in the treatment of diabetic peripheral neuropathy [J]. Journal of applied gynecology and endocrinology, 2017,4(36):65-67.
[18] Huang Pengzhan. Observation of Angelica Sini Decoction in the treatment of diabetic peripheral neuropathy [J]. Shenzhen journal of integrated traditional and western medicine, 2015,25(23):53-54.
[19] Li Chuangao. Clinical observation of Angelica Sini Decoction in the treatment of diabetic peripheral neuropathy [J]. Clinical Journal of Traditional Chinese Medicine,2014,(01):44-45.
[20] Wang Manya. Clinical observation of modified Angelica Sini Decoction in the treatment of diabetic peripheral neuropathy (Yang deficiency and cold coagulation syndrome) [D]. Heilongjiang University of Traditional Chinese Medicine, 2019.
[21] Liu Feng. Clinical observation of modified Angelica Sini Decoction in the treatment of diabetic peripheral neuropathy [D]. Guangzhou University of Chinese Medicine,2008.
[22] Yang Yanling. Clinical observation of integrated Traditional Chinese and Western medicine in the treatment of type 2 diabetic peripheral neuropathy [J]. Beijing Traditional Chinese Medicine, 2007, (07):408-410.
[23] Xue Jun, Hu Feng, Hua Wenjin. Clinical observation of integrated traditional Chinese and western medicine in treating diabetic peripheral neuropathy [J]. Journal of modern integrated traditional Chinese and western medicine, 2010, 19(18):2228-2230.
[24] Yang Liu. Observation on the curative effect of Angelica Sini Decoction in the treatment of diabetic peripheral neuropathy [J]. Journal of Practical Traditional Chinese Medicine, 2018, (04): 409-410.
[25] Chen Hongmei, Wu Jianfang, On South China. Clinical observation of Angelica Sini Decoction in treatment of diabetic peripheral neuropathy [J]. New Traditional Chinese Medicine, 2017,(03): 56-58.