Int J Clin Exp Med 2019;12(4):3364-3375
www.ijcem.com /ISSN:1940-5901/IJCEM0086233

Original Article

Observation of the clinical effects of Danhong injections combined with pitavastatin on blood lipid regulation in patients with ischemic strokes complicated with lipid abnormalities

Yan Xu[1*], Meiling Chen[1*], Quan Xiao[1], Yuyi Zhao[2], Jun Tian[3]

Departments of [1]Pharmacy, [2]Anesthesiology, [3]Clinical Laboratory, Dezhou People's Hospital, Dezhou, Shandong Province, China. [*]Equal contributors and co-first authors.

Received September 30, 2018; Accepted November 29, 2018; Epub April 15, 2019; Published April 30, 2019

Abstract: Objective: The aim of this study was to examine the clinical effects of Danhong injections combined with pitavastatin on blood lipid regulation in patients with ischemic strokes complicated with lipid abnormalities. Methods: A total of 116 patients with ischemic strokes, admitted to the Department of Neurology of Dezhou People's Hospital, from April 2016 to March 2018, were selected and randomly divided into an observation group (58 patients) and control group (58 patients), according to treatment modality. Patients in both groups were given general symptomatic supportive care. The control group was treated with pitavastatin and the observation group was treated with pitavastatin combined with Danhong injections to reduce blood lipids. Then the two groups were compared in therapy effects, blood lipid levels, inteima-media thickness (IMT), inflammatory factors, change of oxidative stress, nerve function, and index levels of laboratory examinations. Results: The observation group showed a significantly higher total effective rate of treatment (93.10%) than the control group (62.06%) (χ^2=16.062, P<0.001). After treatment, the observation group showed significantly lower total cholesterol, triglycerides, and low-density lipoprotein cholesterol than the control group (all P<0.001), as well as significantly higher high-density lipoprotein cholesterol than the control group (P<0.001). No significant differences in IMT (P>0.05) were found. Significantly lower C-reactive protein and fibrinogen was found, compared to the control group (both P<0.001). No differences in oxidized low-density lipoprotein and superoxide dismutase (SOD) were found, compared to before treatment (both P>0.05). Significantly lower ox-LDL was exhibited, compared to the control group (P<0.001), along with significantly higher SOD, compared to the control group (P<0.001). Significantly lower neurological function defect scale scores were found, compared to the control group (P<0.001), as well as significantly higher Barthel indexes (P<0.001). Results also showed significantly lower urinary protein positive rates than the control group (P<0.05), significantly lower serum creatinine, urea nitrogen, leukocyte count, red blood cell counts, and creatine kinase than the control group (all P<0.05). Moreover, significantly lower platelet counts were found, compared to the control group (P<0.05). Conclusion: Danhong injections combined with pitavastatin are effective in blood lipid regulation, significantly inhibiting the inflammatory response of patients, reducing oxidative stress damage, and promoting the recovery of nerve function. Therefore, the clinical effects are significant.

Keywords: Danhong injections, pitavastatin, ischemic strokes, blood lipid levels, oxidative stress

Introduction

Ischemic stroke is a cerebrovascular disease with high incidence in clinic. Studies have shown that, in China, stokes have an annual incidence as high as 212.6/100,000, annual increase of 2.76 million, and an annual death toll of 1.31 million, drawing much clinical attention [1]. The main pathogenesis of this disease includes vessels in local brain tissues suffering spasms, stenosis, and even occlusion for atherosclerosis (AS) and others, resulting in death due to cerebral ischemia and hypoxia [2]. Clinically, patients with this disease often suffer vertigo, diplopia, and even show disturbances of consciousness and death. This disease is highly recurrent, greatly impacting the body and mind [3].

There are many factors inducing ischemic strokes, including lipid abnormalities, increased intima-media thickness (IMT), neuronal apopto-

sis, and increased inflammatory cytokines caused by injury. Lipid abnormalities, especially the decrease of high-density lipoprotein cholesterol (HDL-C), is the leading factor. This is because increased blood viscosity, hematocrit, and coagulation activity cause AS and abscisic of atheromatous plaques in vessel tube. Atheromatous plaques then enter cerebral arteries with blood flow, causing cerebral infarction. The second leading factor is neuron apoptosis. Neuron apoptosis can easily lead to lesions and death of neurons in brain tissues, causing nerve function defects and decreased daily living ability [4]. Recent studies have shown that new risk factors, such as inflammatory response, are closely related to the occurrence of acute cerebral infarction [5].

In the early stages of onset of the disease, medical treatment should be given in time to prevent the development of cerebral ischemia, avoiding further brain damage. In the later stages, specific measures can be taken according to the actual situation of the patient, including etiology, pathogenesis, and onset time [6]. In the past, statins were often used in clinical treatment of the disease after routine treatment. Statins treat the disease by lowering cholesterol production and increment. In statins, pitavastatin is distinguished by its unique urinary excretion rate in urine of less than 2%. It is also featured with non-metabolism, lipid solubility, and rare metabolism of cytochrome P450 (CYP), having certain treatment effects [7]. One study indicated that Danhong injections play an important role in the treatment of cardiovascular and cerebrovascular diseases, such as strokes, and can coordinate therapeutic effects and improve comprehensive therapy effects [8]. In this study, the comprehensive efficacy of Danhong injections combined with others was examined, aiming to provide guidance for clinicians.

Materials and methods

General information

A total of 116 patients with ischemic strokes, admitted to the Department of Neurology of Dezhou People's Hospital, from April 2016 to March 2018, were selected as study objects. Inclusion criteria were: (1) Patients complying with diagnostic guidelines for relevant ischemic strokes released in the 2016 China Stroke Conference; (2) Patients confirmed to be with ischemic strokes through head computed tomography or magnetic resonance imaging; (3) Patients diagnosed with carotid atherosclerosis through carotid ultrasounds; (4) Patients diagnosed with lipid abnormalities through laboratory detection; and (5) Patients that actively participated in this experimental study and provided informed consent [9, 10]. Exclusion criteria were: (1) Patients with acute or chronic inflammation, malignant tumors, or rheumatism; (2) Patients with major trauma or thromboembolism in the past six months; (3) Patients with secondary hyperlipemia for gout, diabetes and others; (4) Patients with severe mental disorders, such as severe depression; and (5) Patients with allergic reactions to the drugs used in this study. The 116 patients were randomly divided into an observation group (58 patients) and control group (58 patients), according to treatment modality. The control group consisted of 36 males and 22 females at 34-85 years old (mean age of (62.15±4.54) years old), with a course of 2-6 hours and an average onset time of (4.38±1.23) hours. In the control group, in terms of the classification of cerebral atherosclerosis, there were 28 patients with bilateral cerebral atherosclerosis and 30 patients with unilateral cerebral atherosclerosis. In terms of complications, there were 29 patients with hypertension and 29 patients with diabetes. In terms of infraction site, there were 25 patients with intra-carotid infarction, 18 patients with brainstem infarction, and 15 patients with mixed infarction. The observation group consisted of 34 males and 24 females at 35-86 years old (mean age of (63.52±5.02) years old), with a course of 2-6 hours and an average onset time of (4.51±1.31) hours. In the observation group, in terms of the classification of atherosclerosis, there were 31 patients with bilateral atherosclerosis and 27 patients with unilateral cerebral atherosclerosis. In terms of complications, there were 31 patients with hypertension and 27 patients with diabetes. In terms of infraction site, there were 26 patients with intra-carotid infarction, 17 patients with brainstem infarction, and 15 patients with mixed infarction. This study was approved by the Ethics Committee of Dezhou People's Hospital and all patients provided informed consent.

Methods

Both groups received regular treatment after admission, including oxygen inhalation and nutritional support. Patients with type 2 diabetes were treated with insulin (Nanjing Xinbai Pharmaceutical Co., Ltd., China, 3 mL) and pa-

Table 1. Comparison of general information

	Control group (n=58)	Observation group (n=58)	$t/\chi^2/H$	P
Average age (year)	62.15±4.54	63.52±5.02	1.542	0.126
Gender (male/female)	36/22	34/24	0.036	0.849
Average onset time (h)	4.38±1.23	4.51±1.31	0.551	0.583
The classification of cerebral atherosclerosis (n, %)				
Bilateral	28 (48.28)	31 (53.45)	0.138	0.710
Unilateral	30 (51.72)	27 (46.55)	0.138	0.710
Complication (n, %)				
Hypertension	29 (50.00)	31 (53.45)	0.035	0.853
Diabetes	29 (50.00)	27 (46.55)	0.035	0.853
Infraction site (n, %)				
Intra-carotid infarction	25 (43.10)	26 (44.83)	0.035	0.852
Brainstem infarction	18 (31.03)	17 (29.31)	0.041	0.840
Mixed infarction	15 (25.86)	15 (25.86)	0.000	1.000

Table 2. Comparison of therapy effects (n, %)

	Control group (n=58)	Observation group (n=58)	x^2	P
Recovered	0 (0.00)	0 (0.00)		
Obviously effective	18 (31.03)	35 (60.34)		
Effective	18 (31.03)	19 (37.76)		
Non-effective	22 (37.93)	4 (6.90)		
Total effective rate	62.06	93.10	16.062	<0.001

tients with hypertension were treated with captopril tablets (Changzhou Pharmaceutical Factory Co., Ltd., China, 25 mg). Those patients experienced a 2-week washout period, during which drugs for anticoagulation, thrombolysis, or defibration were discontinued. After the washout period, the control group was further treated with pitavastatin (Japan Kowa Company, Ltd, Nagoya Factory, 2 mg) via oral administration before bedtime at 20 mg each time, once a day. Based on the treatment for the control group, the observation group was additionally treated with Danhong injections in doses as follows: 20 mL of Danhong injections (China Shandong Danhong Pharmaceutical Co., Ltd., Z20026866, 60 mL) was added into 250 mL of 0.9% sodium chloride solution (Guangdong Stsuka harmaceutical Co., Ltd., 500 mL) for intravenous drip at a rate of 40 to 60 drops/minute, once a day. One course lasted 3 months. Efficacy of the treatment was evaluated after two consecutive courses.

Observation indexes

The two groups were compared in total effective rates of treatment. They were compared in blood lipid levels, such as HDL-C, total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C), before and after treatment. The two groups were compared in hemorheology indexes, before and after treatment. They were compared in IMT, before and after treatment. They were compared in inflammatory factors, C-reactive protein (CRP), fibrinogen (Fbg) levels, and relevant oxidative stress indexes, such as oxidative stress oxidized low-density lipoprotein (ox-LDL) and superoxide dismutase (SOD), before and after treatment. The two groups were compared in neurological function defect scale (NFDS) scores, before and after treatment, and Barthel indexes [10, 11]. Finally, they were also compared in index levels of laboratory examinations, before and after treatment.

Efficacy criterion and detection methods

Therapy effects of patients were evaluated based on NFDS scores and clinical symptoms. Effects were divided into the following [11].

(1) Recovered: NFDS scores were reduced by more than 90% and most or all of the symptoms disappeared; (2) Obviously effective: NFDS scores were reduced by 40% to 89%; (3) Effective: NFDS scores were reduced by 18% to 39%; (4) Non-effective: NFDS scores were not reduced obviously and the symptoms did not change. The total effective rate of treatment = (the number of recovered patients + the number of patients with obviously effective + the

Table 3. Comparison of blood lipid levels ($\bar{x}$ ± sd, mmol/L)

	Control group (n=58)	Observation group (n=58)	t	P
TC				
Before treatment	6.32 ± 0.84	6.33 ± 0.90	0.061	0.962
After treatment	5.23 ± 1.19###	4.12 ± 1.22###	4.741	<0.001
TG				
Before treatment	2.54 ± 0.65	2.53 ± 0.59	0.081	0.932
After treatment	2.13 ± 0.61###	1.62 ± 0.55###	4.521	<0.001
LDL-C				
Before treatment	4.28 ± 0.56	4.30 ± 0.72	0.161	0.873
After treatment	3.23 ± 0.75###	2.57 ± 0.67###	4.781	<0.001
HDL-C				
Before treatment	0.91 ± 0.23	0.93 ± 0.20	0.481	0.632
After treatment	1.16 ± 0.38###	1.50 ± 0.27###	5.311	<0.001

Note: Compared before treatment, ###P<0.001. TC, total cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

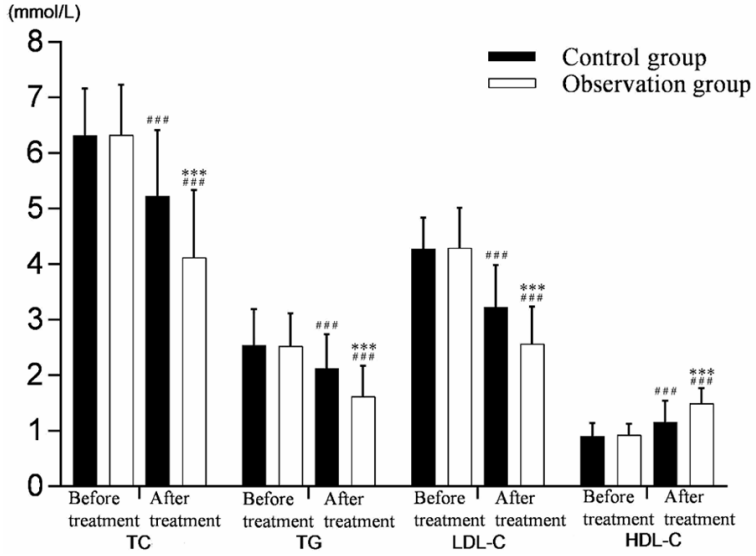

Figure 1. Comparison of blood lipid levels. ***P<0.001 compared with the control group; ###P<0.001 compared with that before treatment. TC, total cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

number of patients with effective)/the total number of patients * 100%.

Statistical methods

Statistical data were analyzed using SPSS 21.0 professional statistical software. Measurement data are expressed as mean ± standard deviation. Independent samples were processed with t-tests, while comparison of patients before and after testing was processed with paired t-tests. Enumeration data are expressed as the rate (n%) and processed with Chi-squared test. P<0.05 indicates statistical significance.

Results

Comparison of general information

There were no significant differences in gender, age, onset time, atherosclerosis classification, and complication type between the two groups (all P>0.05). See **Table 1** for details.

Comparison of therapy effects

The observation group showed a total effective rate of treatment of 93.10%, while the control group showed a total effective rate of 62.06%. The former was significantly higher than the latter (χ^2=16.062, P<0.001). See **Table 2** for details.

Comparison of blood lipid levels

The two groups showed no significant differences in blood lipid levels before treatment (all P>0.05). After treatment, the two groups showed significantly lower TC, TG, and LDL-C than before treatment (all P<0.001) and significantly higher HDL-C than before treatment (both P<0.001). The observation group showed significantly lower TC (4.12±1.22), TG (1.62±0.55), and LDL-C (2.57±0.67) than the control group (5.23±1.19, 2.13±0.61, and 3.23±0.75) (all P<0.001) and significantly higher HDL-C (1.50±0.27) than the control group (1.16±0.38) (P<0.001). See **Table 3** and **Figure 1** for details.

Comparison of IMT

The two groups showed no significant differences in IMT in the left common carotid artery,

Table 4. Comparison of IMT ($\bar{x}$ ± sd, mm)

	Control group (n=58)	Observation group (n=58)	t	P
Left common carotid artery				
Before treatment	6.09 ± 0.32	6.33 ± 0.90	0.914	0.060
After treatment	5.23 ± 1.19###	5.12 ± 1.22###	0.492	0.624
Right common carotid artery				
Before treatment	2.54 ± 0.65	2.53 ± 0.59	0.087	0.931
After treatment	2.13 ± 0.61###	2.02 ± 0.55###	1.020	0.310
Left internal carotid artery				
Before treatment	4.28 ± 0.56	4.30 ± 0.72	0.167	0.877
After treatment	3.23 ± 0.75###	3.07 ± 0.67###	1.212	0.228
Right internal carotid artery				
Before treatment	1.16 ± 0.38	1.19 ± 0.27	0.490	0.625
After treatment	0.91 ± 0.23###	0.93 ± 0.20###	0.500	0.618

Note: Compared before treatment, ###P<0.001.

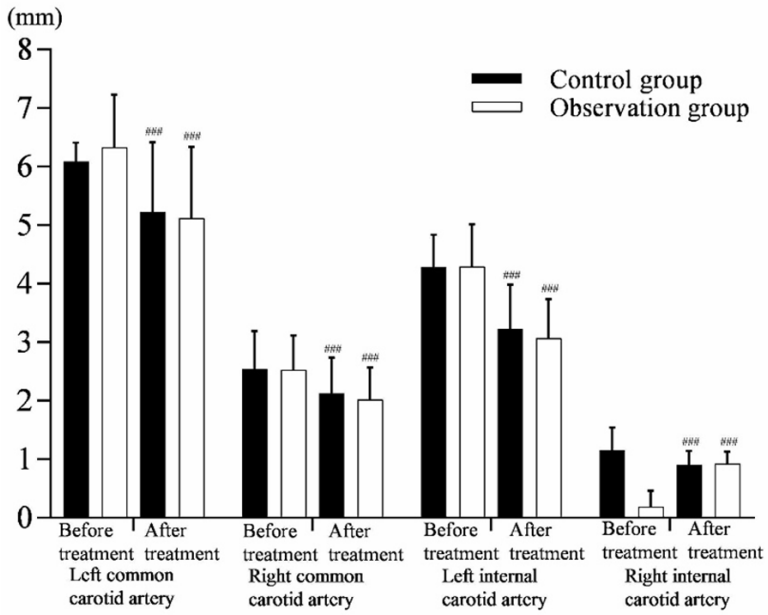

Figure 2. Comparison of IMT. ###P<0.001 compared with before treatment. IMT, intima-media thickness.

right common carotid artery, left internal carotid artery, and right internal carotid artery before treatment (all P>0.05). After treatment, the two groups showed smaller IMT than before treatment (all P<0.001), but the there were no significant differences between the two groups (all P>0.05). See **Table 4** and **Figure 2** for details.

Comparison of hemorheology indexes

There were no significant differences in hemorheology indexes between the two groups before treatment (all P>0.05). After treatment, the two groups showed significantly lower hemorheology indexes, such as whole blood viscosity, plasma viscosity, hematocrit, and red blood cell indexes, than before treatment (all P<0.001). The observation group showed significantly lower hemorheology indexes than the control group (all P<0.001). See **Table 5** and **Figure 3** for details.

Comparison of inflammatory factors and relevant oxidative stress indexes

Before treatment, the two groups showed no significant differences in CRP, Fbg levels, and relevant oxidative stress indexes-oxidative stress ox-LDL and SOD (all P>0.05). After treatment, the observation group showed no significant differences in ox-LDL and SOD, compared to before treatment (both P>0.05), but significantly lower CRP and Fbg than before treatment (both P<0.001). After treatment, the control group showed significantly higher ox-LDL than before treatment (P<0.001) and significantly lower CRP, Fbg, and SOD than before treatment (all P< 0.001). The observation group showed significantly lower CRP, Fbg, and ox-LDL than the control group (all P< 0.001) and significantly higher SOD levels than the control group (P<0.001). See **Table 6** and **Figure 4** for details.

Comparison of NFDS scores and the Barthel index

Before treatment, the two groups showed no significant differences in NFDS scores and Barthel index scores (both P>0.05). After treatment, the two groups showed lower NFDS scores than before treatment (both P<0.001) and higher Barthel index scores than before

Table 5. Comparison of hemorheology indexes ($\bar{x}$ ± sd)

	Control group (n=58)	Observation group (n=58)	t	P
Whole blood viscosity low cut (mpa*s)				
Before treatment	16.75 ± 2.13	17.33 ± 1.76	1.599	0.113
After treatment	13.66 ± 1.78###	10.12 ± 1.55###	11.422	<0.001
Whole blood viscosity high cut (mpa*s)				
Before treatment	7.85 ± 1.40	7.84 ± 1.37	0.039	0.969
After treatment	6.41 ± 0.72###	5.37 ± 0.58###	8.567	<0.001
Plasma viscosity (mpa*s)				
Before treatment	1.75 ± 0.86	1.84 ± 0.80	0.584	0.561
After treatment	1.67 ± 0.85###	1.21 ± 0.37###	3.779	<0.001
Hematocrit (%)				
Before treatment	47.38 ± 3.24	48.37 ± 3.13	1.674	0.097
After treatment	45.21 ± 2.01###	43.21 ± 2.42###	4.842	<0.001
Red blood cell				
Before treatment	1.48 ± 0.43	1.47 ± 0.45	0.122	0.903
After treatment	1.36 ± 0.15###	1.01 ± 0.34###	7.173	<0.001

Note: Compared before treatment, ###P<0.001.

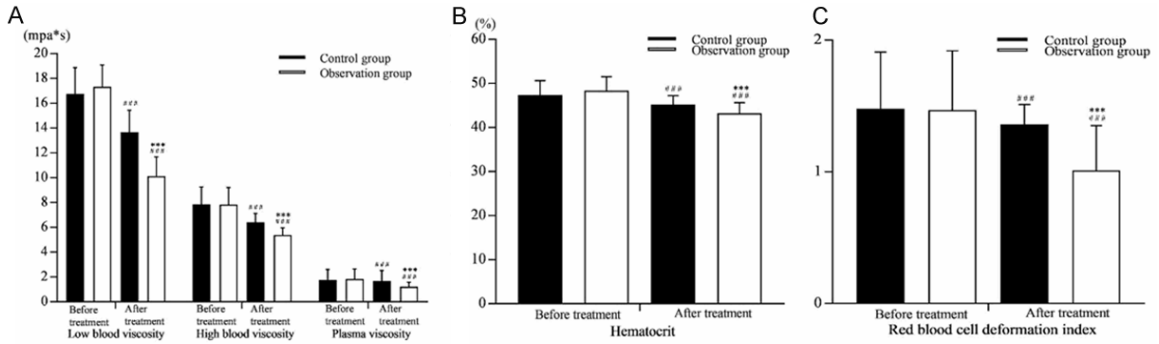

Figure 3. Comparison of hemorheology indexes. ***P<0.001 compared with the control group; ###P<0.001 compared with that before treatment.

treatment (both P<0.001). The observation group showed significantly lower NFDS sores than the control group and significantly higher Barthel index scores than the control group (both P<0.001). See **Table 7** and **Figure 5** for details.

Comparison of index levels of laboratory examinations

Before treatment, the two groups showed no significant differences in urinary protein positive rates, serum creatinine, urea nitrogen, leukocyte counts, red blood cell counts, creatine kinase, and platelet counts (all P>0.05). After treatment, the observation group showed higher urea nitrogen, creatine kinase, and platelet counts than those before treatment (all P< 0.05), as well as no significant differences in serum creatinine, leukocyte counts, and red blood cell counts with those before treatment (all P>0.05). The control group showed higher serum creatinine, urea nitrogen, leukocyte counts, red blood cell counts, creatine kinase, and platelet counts than those before treatment (all P<0.05). The observation group showed significantly lower urinary protein positive rates than the control group (P<0.05), significantly lower serum creatinine, urea nitrogen, leukocyte counts, red blood cell counts, and creatine kinase platelet counts than the control

Table 6. Comparison of inflammatory factors and relevant oxidative stress indexes ($\bar{x}$ ± sd)

	Control group (n=58)	Observation group (n=58)	t	P
CRP (mg/L)				
Before treatment	2.52 ± 1.09	2.50 ± 1.06	0.100	0.920
After treatment	2.32 ± 1.03###	1.85 ± 0.81###	3.662	<0.001
Fbg (g/L)				
Before treatment	4.06 ± 1.34	4.02 ±1.56	0.148	0.883
After treatment	3.86 ± 1.08###	3.20 ± 0.85###	3.657	<0.001
ox-LDL (μg/dL)				
Before treatment	15.05 ± 4.34	15.12 ± 4.18	0.089	0.930
After treatment	18.24 ± 4.78###	15.27 ± 3.90	3.666	<0.001
SOD (U/mL)				
Before treatment	19.93 ± 7.70	20.09 ± 7.92	0.110	0.912
After treatment	17.34 ± 6.87###	19.78 ± 7.52	3.619	<0.001

Note: Compared before treatment, ###P<0.001. CRP, C-reactive protein; Fbg, fibrinogen; ox-LDL, oxidized low density lipoprotein; SOD, superoxide dismutase.

group (all P<0.05). See **Table 8** and **Figure 6** for details.

Discussion

Ischemic stroke is a common cerebrovascular disease in Western medicine. Because lipid abnormalities are the main cause of the disease and indicate the severity of the disease, serum lipid levels can be used as a key indicator for assessment of therapy effects [12]. Many Chinese and foreign studies have indicated that the rational use of statins for lipid regulation has certain effects on treatment of ischemic strokes. Therefore, many studies have been carried out on the selection of statins, with pitavastatin, a hydroxymethyl glutaryl coenzyme A reductase inhibitor, widely recognized [13-16]. Pharmacological research has shown that the mechanisms of pitavastatin include the inhabitation of cholesterol synthesis for the regulation of cholesterol metabolism and reduction of serum cholesterol levels in patients. In addition, pitavastatin can improve vasodilation, increase blood supply, and act as anticoagulation substance to correct the imbalance of coagulation function in the body [17]. Studies have shown that the efficacy of pitavastatin in reducing blood lipid is positively correlated with the dose. When the dose is increased by 1 time, the decrease in blood lipids is increased by 5% to 7%. However, as the dose increases, incidence of adverse drug reactions increases. Therefore, if the dose is high, the patient may suffer problems, including transaminase elevation and elevation of zymogram, such as myositis, suggesting that the drug has side effects involving the livers of patients. Naturally, the application of pitavastatin has been restricted [18]. Therefore, the purpose of this study was to find measures to reduce the dose of pitavastatin in combination use, while maintaining its high efficacy. This is the key to eliminating its restrictions.

In recent years, Traditional Chinese Medicine has developed rapidly. There are more and more successful examples of combinations with Western medicine in clinical treatment. However, reports concerning the combination of integrated Traditional Chinese and Western medicine in the treatment of ischemic strokes are extremely rare [19]. Ischemic strokes are called “strokes” in Traditional Chinese Medicine. The key in treatment is promoting blood circulation to remove blood stasis, achieving the main role of reducing blood lipids [20]. In recent years, it has not been uncommon to adopt Danhong injections alone for ischemic strokes. As a compound preparation in Traditional Chinese Medicine, it has been proven to have a certain effect, especially in the protection of nerve function [21]. Studies have confirmed that the ingredients of Danhong injections include effective components extracted from two Traditional Chinese Medicines, salvia miltiorrhiza and safflower. The effective components of salvia miltiorrhiza include tanshinone and salvianolic acid, while the effective components of safflower include carthamin and safflor yellow [22]. Therefore, reducing the dose of pitavastatin was achieved by combining pitavastatin and Danhong injections. Additionally, the comprehensive efficacy of combination of pitavastatin and Danhong injections increases in return. Results of the present study reveal that the observation group showed significantly higher total efficiency rates, compared to the control group, as well as significantly lower NFDS scores and significantly higher Barthel index scores, compared to the control group, after treatment. These results suggest that Danhong injections have the advantage of protecting nerve function.

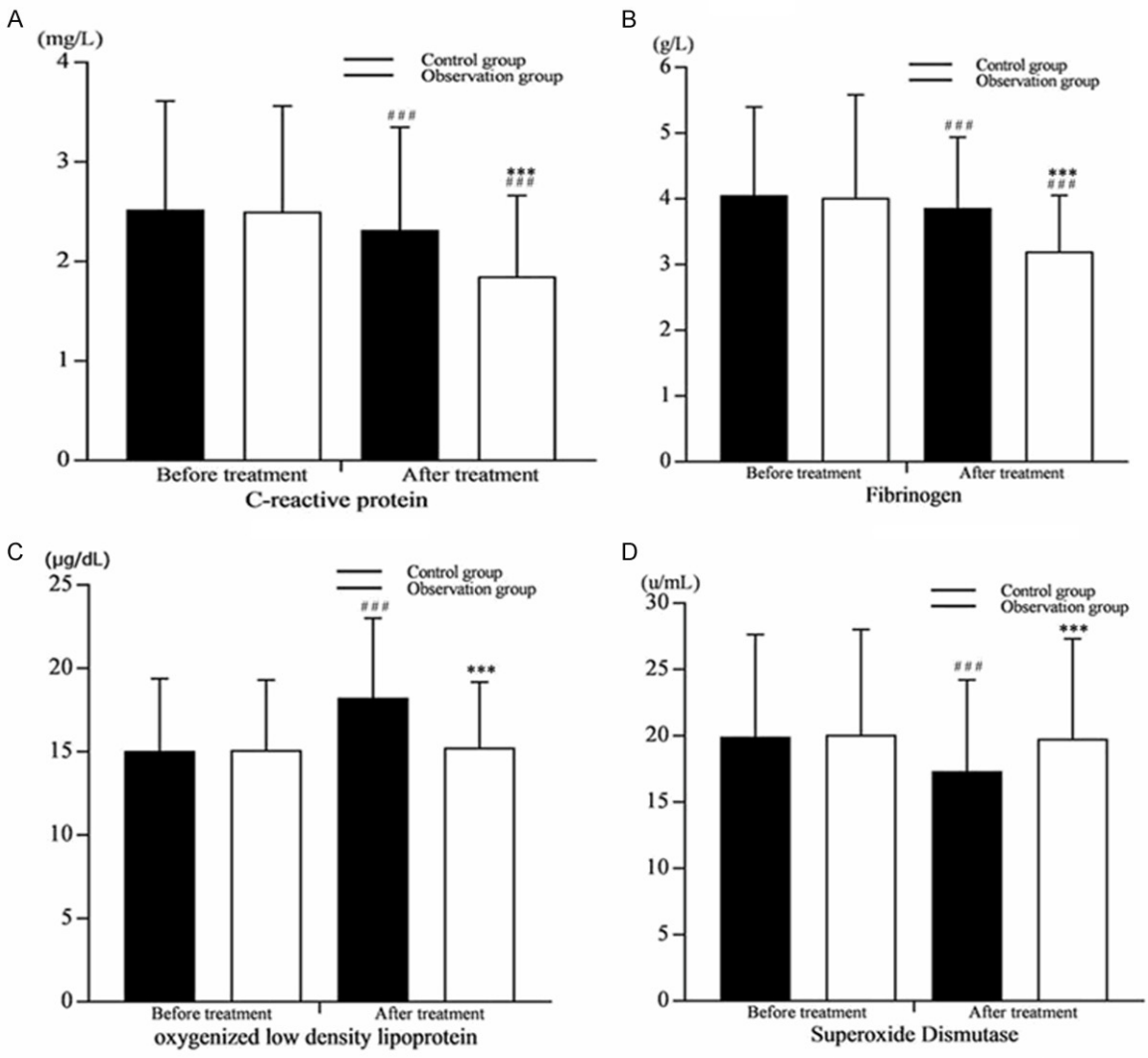

Figure 4. Comparison of inflammatory factors and oxidative stress related indexes. ***P<0.001 compared with the control group; ###P<0.001 compared with that before treatment.

Table 7. Comparison of NFDS scores and Barthel index ($\bar{x}$ ± sd)

	Control group (n=58)	Observation group (n=58)	t	P
NFDS score				
Before treatment	17.32 ± 8.24	18.33 ± 7.90	0.674	0.502
After treatment	10.21 ± 4.19###	6.44 ± 3.21###	5.440	<0.001
Barthel index				
Before treatment	26.54 ± 10.15	26.53±10.29	0.005	0.996
After treatment	50.13 ± 10.54###	68.62 ± 15.61###	7.476	<0.001

Note: Compared before treatment, ###P<0.001. NFDS, neurological function defect scale.

This may be because safflower enhances the brain's ability to resist ischemia by improving microcirculation, thus protecting the nerve function of the brain [23].

In this study, before treatment, the two groups showed elevated TC, TG, LDL-C, and decreased HDL-C, suggesting that lipid abnormalities are the main marker of the disease. After treatment, the observation group showed significantly lower total TC, TG, LDL-C, and higher HDL-C than the control group. The observation group also showed higher SOD levels and lower ox-LDL levels than the control group. The main reason was that salvia prevents platelet aggregation by controlling the activation of phosphodiesterase activity. It reduces malignant coagulation and increases the concentration of pros-

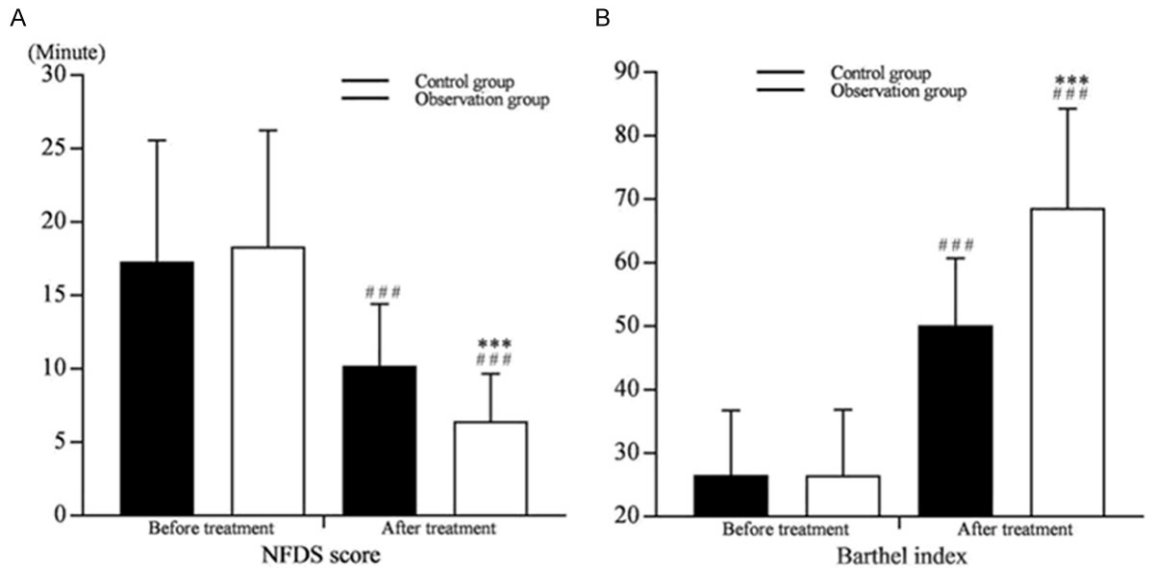

Figure 5. Comparison of NFDS scores and Barthel index. ***P<0.001 compared with the control group; ###P<0.001 compared with that before treatment. NFDS, neurological function defect scale.

Table 8. Comparison of index levels of laboratory examinations ($\bar{x}$ ± sd, (n, %))

	Control group (n=58)	Observation group (n=58)	t	P
Urinary protein positive rate (%)	12 (20.69)	4 (6.90)	4.640	0.031
Serum creatinine (μmol/L)				
Before treatment	67.06 ± 15.12	68.02 ± 15.22	0.341	0.734
After treatment	78.86 ± 29.08#	68.40 ± 10.85	2.567	0.012
Urea nitrogen (mmol/L)				
Before treatment	4.32 ± 1.63	4.35 ± 1.64	0.099	0.922
After treatment	5.91 ± 2.58#	5.01 ± 1.64#	2.242	0.027
Leukocyte count (*10^9/L)				
Before treatment	74.93 ± 20.70	74.09 ± 20.92	0.217	0.828
After treatment	89.34 ± 31.23#	75.78 ± 31.34	2.334	0.021
Red blood cell count (*10^{12}/L)				
Before treatment	6.67 ± 1.17	6.81 ± 1.22	0.631	0.530
After treatment	7.90 ± 1.90#	7.12 ± 1.88	2.222	0.028
Creatine kinase (U/L)				
Before treatment	77.34 ± 45.12	78.12 ± 45.53	0.093	0.926
After treatment	107.12 ± 60.23#	86.34 ± 45.20#	2.102	0.038
Platelet count (*10^9/L)				
Before treatment	201.12 ± 42.18	202.34 ± 43.82	0.153	0.879
After treatment	246.35 ± 42.23#	215.27 ± 45.78#	3.800	<0.001

Note: Compared before treatment, #P<0.001.

tacyclin by activating prostacyclin synthase, thereby promoting vasodilation and SOD activity recovery and improving the oxidative stress ability [24].

Hemorheology also had a significant predictive effect. Before treatment, the two groups showed increased whole blood viscosity, plasma viscosity, hematocrit, and red blood cell index-

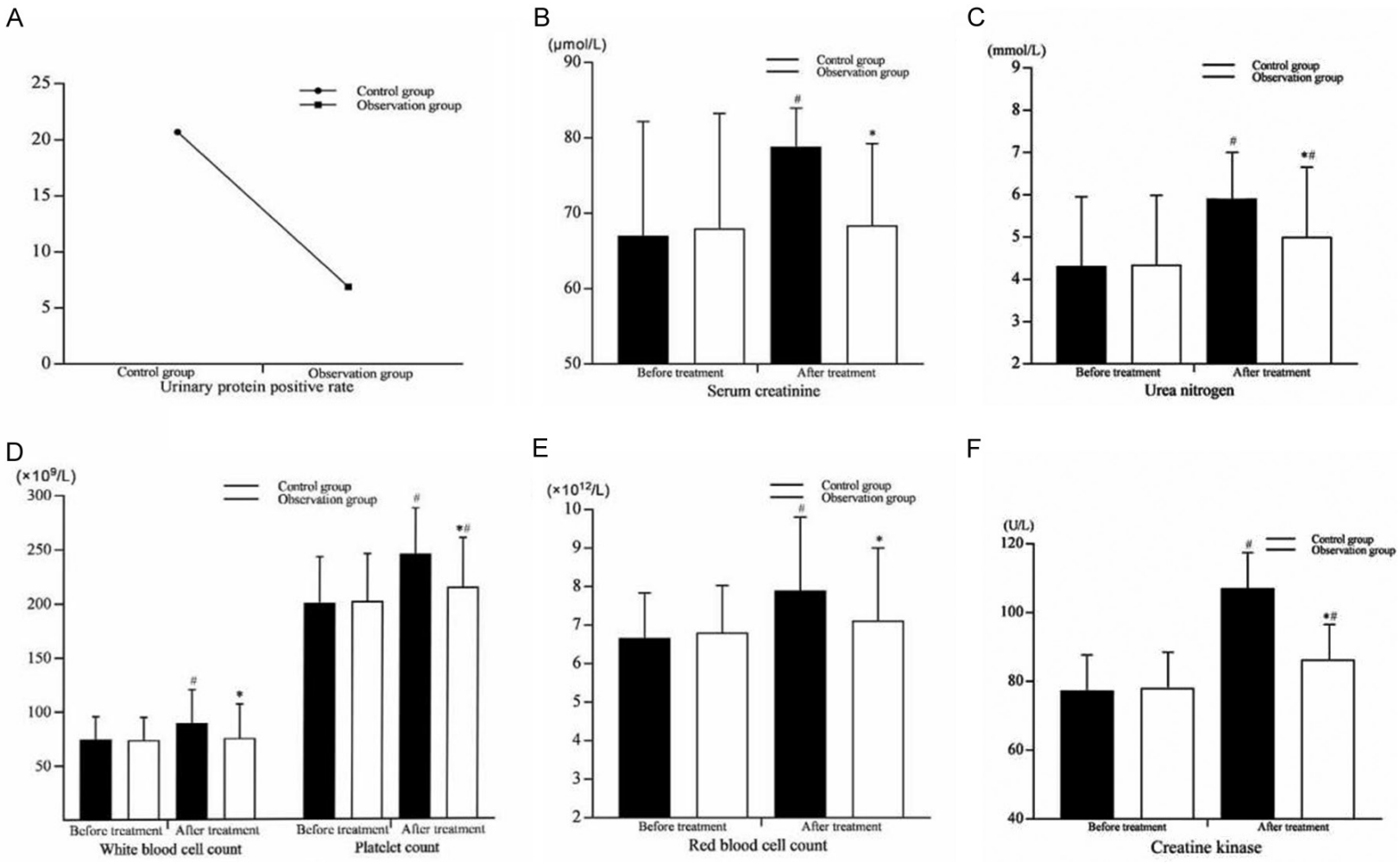

Figure 6. Comparison of laboratory test indicators. *P<0.05 compared with the control group; #P<0.05 compared with that before treatment.

es, causing the danger of increasing atherosclerosis. After treatment, the observation group showed lower indexes than the control group, due to the fact that salvia prevented platelet aggregation by controlling the activation of phosphodiesterase activity, reduced malignant coagulation, and improved the hemodynamics, such as blood viscosity decreases and erythrocyte deformability enhancement.

Inflammatory response has a good predictive effect in many diseases. Nerve cell damage and vascular tube wall sclerosis can cause inflammatory response. Therefore, this study also selected inflammatory factors, CRP and Fbg. Results of the study show that, after treatment, the observation group showed significantly higher CRP and Fbg levels than the control group, confirming the combined efficacy of drug combination [25]. Moreover, the observation group showed significantly lower urinary protein positive rates, serum creatinine, urea nitrogen, leukocyte counts, red blood cell counts, creatine kinase, and platelet counts than the control group, consistent with the above findings [26]. However, there were no statistical differences in IMT between the two groups, which may have been related to the short observation times.

The innovation of this study was that this drug combination reduced the dose of pitavastatin with side effects, increased comprehensive efficacy, and protected nerve function. The limitation of this study was that there was no data confirming the elimination of side effects after the drug combination.

In summary, Danhong injections, in combination with pitavastatin, show good blood lipid regulation effects, significantly inhibiting inflammatory response, reducing oxidative stress, and promoting the recovery of nerve function. Therefore, this method is worthy of promotion in clinic.

Disclosure of conflict of interest

None.

Address correspondence to: Jun Tian, Department of Clinical Laboratory, Dezhou People's Hospital, No.1751 Xinhu Street, Decheng District, Dezhou 253014, Shandong Province, China. Tel: +86-0534-2265591; E-mail: tianjun3619@163.com

References

[1] Ashburner JM, Go AS, Chang Y, Fang MC, Fredman L, Applebaum KM and Singer DE. Effect of diabetes and glycemic control on ischemic stroke risk in af patients: atria study. J Am Coll Cardiol 2016; 67: 239-47.

[2] Bang OY. Clinical trials of adult stem cell therapy in patients with ischemic stroke. J Clin Neurol 2016; 12: 14-20.

[3] Zerna C, Hegedus J and Hill MD. Evolving treatments for acute ischemic stroke. Circ Res 2016; 118: 1425.

[4] Liao SH, Luo CX, Cao BZ, Hu HQ, Wang SX, Yue HL, Chen L and Zhou ZH. Endothelial progenitor cells for ischemic stroke: update on basic research and application. Stem Cells Int 2017; 2017: 2193432.

[5] Hoy SM. Pitavastatin: a review in hypercholesterolemia. Am J Cardiovasc Drugs 2017; 17: 157.

[6] Gerschenfeld G, Muresan IP, Blanc R, Obadia M, Abrivard M, Piotin M and Alamowitch S. Two paradigms for endovascular thrombectomy after intravenous thrombolysis for acute ischemic stroke. JAMA Neurol 2017; 74: 549.

[7] Wu YL, Saver JL, Chen PC, Lee JD, Wang HH, Rao NM, Meng L and Ovbiagele B. Effect of statin use on clinical outcomes in ischemic stroke patients with atrial fibrillation. Medicine 2017; 96: e5918.

[8] Wan JY, Wan HF, Yang RB, Wan HT, Yang JH, He Y and Zhou HF. Protective effect of Danhong injection combined with Naoxintong capsule on cerebral ischemia-reperfusion injury in rats. J Ethnopharmacol 2018; 211: 348-357.

[9] Sachdev P, Kalaria R, O'Brien J, Skoog I, Alladi S, Black SE, Blacker D, Blazer DG, Chen C and Chui H. Diagnostic criteria for vascular cognitive disorders: a VASCOG statement. Alzheimer Dis Assoc Disord 2014; 28: 206.

[10] Huang CH, Huang YY and Hsu BR. Pitavastatin improves glycated hemoglobin in patients with poorly controlled type 2 diabetes. J Diabetes Investig 2016; 7: 769-76.

[11] Qian J, Zhao XP, Wang WT, Zhang SJ, Hong ZP, Chen XL, Zhao ZY, Hao CH, Wang CC, Lu SH, Zhao BC and Wang Y. Transcriptomic study reveals recovery of impaired astrocytes contribute to neuroprotective effects of danhong injection against cerebral ischemia/reperfusion-induced injury. Frontiers in Pharmacology 2018; 9.

[12] Toribio M, Fitch KV, Sanchez L, Burdo TH, Williams KC, Sponseller CA, Mccurdy PM, Aberg JA, Zanni MV and Grinspoon SK. Effects of pitavastatin and pravastatin on markers of immune activation and arterial inflammation in HIV. Aids 2017; 31: 797.

[13] Lu G, He Q, Shen Y and Cao F. Potential biomarkers for predicting hemorrhagic transformation of ischemic stroke. Int J Neurosci 2018; 128: 79-89.
[14] Fan H, Li M, Yu L, Jin W, Yang J, Zhang Y and Wan H. Effects of Danhong injection on platelet aggregation in hyperlipidemia rats. J Ethnopharmacol 2018; 212: 67-73.
[15] Xu J, Tang LY, Zhang Q, Wei J, Xian MH, Zhao Y, Jia Q, Li X, Zhang Y, Zhao Y, Wu HW and Yang HJ. Relative quantification of neuronal polar lipids by UPLC-MS reveals the brain protection mechanism of Danhong injection. Rsc Advances 2017; 7: 45746-45756.
[16] Kim J, Lee HS, Nam CM and Heo JH. Effects of statin intensity and adherence on the long-term prognosis after acute ischemic stroke. Stroke 2017; 48: 2723-2730.
[17] Yum KS, Chang JY, Jeong WJ, Lee S, Jeong JH, Yeo MJ, Hong JH, Park HK, Chung I and Kim BJ. Effect of statin on progression of symptomatic basilar artery stenosis and subsequent ischemic stroke. PLoS One 2017; 12: e0183798.
[18] Florentin M and Elisaf MS. Statin therapy and risk of intracranial hemorrhage in patients with ischemic stroke. Drug Saf 2017; 40: 851-853.
[19] Lin FJ, Lin HW and Ho YF. Effect of statin intensity on the risk of epilepsy after ischaemic stroke: real-world evidence from population-based health claims. CNS Drugs 2018; 367-376.
[20] Flint AC, Conell C, Ren X, Kamel H, Chan SL, Rao VA and Johnston SC. Statin adherence is associated with reduced recurrent stroke risk in patients with or without atrial fibrillation. Stroke 2017; 48: 1788.
[21] Nakhjavan-Shahraki B, Yousefifard M, Ataei N, Baikpour M, Ataei F, Bazargani B, Abbasi A, Ghelichkhani P, Javidilarijani F and Hosseini M. Accuracy of cystatin C in prediction of acute kidney injury in children; serum or urine levels: which one works better? A systematic review and meta-analysis. BMC Nephrol 2017; 18: 120.
[22] Ma MT, Cullinane C, Imberti C, Baguña Torres J, Terry SY, Roselt P, Hicks RJ, Blower PJ. New Tris(hydroxypyridinone) bifunctional chelators containing isothiocyanate groups provide a versatile platform for rapid one-step labeling and PET imaging with(68)Ga(3.). Bioconjug Chem 2016; 27: 309-318.
[23] Reith C and Armitage J. Management of residual risk after statin therapy. Atherosclerosis 2016; 245: 161-170.
[24] Mason RP, Sherratt SC and Jacob RF. Eicosapentaenoic acid inhibits oxidation of apob-containing lipoprotein particles of different size in vitro when administered alone or in combination with atorvastatin active metabolite compared with other triglyceride-lowering agents. J Cardiovasc Pharmacol 2016; 68: 33-40.
[25] Tombuloglu H, Ozcan I, Tombuloglu G, Sakcali S and Unver T. Aquaporins in boron-tolerant barley: identification, characterization, and expression analysis. Plant Molecular Biology Reporter 2016; 34: 374-386.
[26] Zhen H, Wang H, Fan GW, Zhang H, Wang XY, Mao JY, Zhao YQ, An Y, Huang YH and Li C, Chang LY, Chu XM, Li L, Li YF, Zhang Y and Qin GJ. Effect of danhong injection on the mobilisation of endothelial progenitor cells to vascular repair after percutaneous coronary intervention: a randomised controlled trial. Lancet 2016; 388: S34-S34.