

Therapeutic effect of Danhong injection on diabetic patients with cerebral infarction and its influence on vascular endothelial function and hemodynamics

Qiang Chi^{1*}, Lin Wang² and Qin Zhang³

¹Health Management Center, Qingdao Chengyang District People's Hospital, Qingdao, China

²Endocrinology Department, Qingdao Chengyang District People's Hospital, Qingdao, China

³Neurology Department, Qingdao Chengyang District People's Hospital, Qingdao, China

Abstract: To investigate the therapeutic effect of Danhong injection on diabetic patients with cerebral infarction and its influence on vascular endothelial function and hemodynamic level. A total of 100 diabetic patients with cerebral infarction admitted to our hospital from November 2019 to November 2020 were identified as the research subjects and randomly divided into a control group given routine treatment and a study group treated with Danhong injection, with 50 cases in each group. The efficiency of the two groups on vascular endothelial function, blood glucose level, National Institute of Health Stroke Scale (NIHSS) score, the incidence of adverse reactions, and hemodynamic indicators were compared. Most (98%) of patients in the study group displayed effective outcomes, which was significantly better than that in the control group. The study group outperformed the control study group in the vascular endothelial function, blood glucose level, NIHSS score and hemodynamic indicators ($P < 0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$). Danhong injection obtains a promising therapeutic effect on diabetic patients with cerebral infarction, as it significantly improves the vascular endothelial function and hemodynamic level.

Keywords: Diabetes with cerebral infarction, Danhong injection, efficiency, vascular endothelial function, hemodynamics.

INTRODUCTION

Currently, the aging of Chinese society and the changes in people's diets and lifestyles have led to an increasing number of people with diabetes in China (Cao *et al.*, 2019). Diabetes mellitus is one of the common metabolic diseases clinically with the main symptom of chronic hyperglycemia (Sreedharan and Abdelmalak, 2018). It is featured by a high incidence of complications, which impairs multiple tissues and organs and causing damage to the central nervous system (DeCarlo and Wallia, 2019). Due to the prevalence of blood stickiness associated with disorders of insulin secretion in diabetic patients, they are at increased risk of developing cerebral infarction which is one of the leading causes of death in diabetic patients (Yuan *et al.*, 2020). Danhong injection consists of two components, flower of honghua (*Flos Carthami Tinctorii*) and roots of danshen (*Radix Salvia Miltiorrhizae*) (Dai *et al.*, 2020; Feng *et al.*, 2019). Modern pharmacological studies have also confirmed that it has antioxidant effects, inhibits vascular smooth muscle hyperplasia, protects vascular endothelial cells, and regulates lipid metabolism. Danhong injection can activate blood circulation by removing blood stasis to protect vascular endothelial cell formation and improve microcirculation and anticoagulation (Bi *et al.*, 2019; Zhang *et al.*, 2020). Thus, it demonstrates great potential in the treatment of various

cardiovascular and cerebrovascular diseases such as coronary heart disease, angina pectoris, and cerebral thrombosis, and therefore merits extensive clinical application (Shi *et al.*, 2019; Zhou *et al.*, 2019; Zhu *et al.*, 2019). In this paper, we aim to analyze the effect of Danhong injection in the treatment of diabetic patients with cerebral infarction and its influence on vascular endothelial function and hemodynamic level, as shown as follows.

MATERIALS AND METHODS

General information

A total of 100 diabetic inpatients with cerebral infarction treated from November 2019 to November 2020 were selected as the subjects and randomly divided into control group and study group, with 50 cases in each group. This paper was ethically approved by the ethics committee of Qingdao Chengyang District People's Hospital (Approval No. of Ethics Committee: NYS2018-0439).

Inclusion criteria

(1) Patients who met the diagnostic criteria of the Chinese Guidelines for the Prevention and Treatment of Diabetes (Wan *et al.*, 2020); (2) Patients who met the diagnostic criteria for cerebral infarction established by the Academic Conference on Cerebrovascular Disease Pathology. (3) Patients with relevant complications confirmed by cranial CT. (4) This study was approved by

*Corresponding author: e-mail: chichenxintian@163.com

the Medical Ethics Committee of the hospital and both patients and their family members signed the study consent form.

Exclusion criteria

(1) Patients with severe liver and kidney dysfunction; (2) Patients with active bleeding. (3) Patients who were allergic to the test drug. (4) Patients with mental illness.

Methods

Both groups received treatment of insulin therapy, and various basic treatment such as blood glucose control, infection control, blood pressure control and diet control was given (Liu *et al.*, 2019; Suzuki *et al.*, 2019). The treatment spanned three weeks to improve vasodilation and endothelial function.

Patients in the control group received conventional treatment and were given oral administration of butylphthalide capsules (SFDA Approval No.: H20050299; Shiyao Group NBP Pharmaceutical Co., Ltd.; 0.1g*24s) before meals, 0.2g per time, 3 times per day, and intravenous injection of Qianlie injection, 10μg per time, 3 times per day. 100 mg aspirin (SFDA Approval No.: H44021139, Guangdong Jiuming Pharmaceutical Co., Ltd., 100mg *30 tablets) was also given to patients in the control group daily to inhibit platelet aggregation. Danshen injection (SFDA Approval No.: Z51021303; Sichuan Shenghe Pharmaceutical Co., Ltd.; 10ml *5 vials) and 40ml of 0.9% normal saline were also administered through intravenous infusion once a day for three weeks (Kim *et al.*, 2018).

In the study group, patients were given Danhong injection (SFDA Approval No.: Z20026866; Heze Buchang Pharmaceutical Co., Ltd.; 10ml *6 vials/box) on the basis of conventional treatment and 40ml of 0.9% normal saline was also given through intravenous infusion once a day for three weeks. The efficiency of the two groups was compared.

Observation on indicators

The efficiency of patients was classified into three levels, namely, significantly effective, effective, and ineffective. The disappearance of clinical symptoms and a reduction of neurological deficit scores over 85% are considered significantly effective. Alleviated clinical symptoms and a reduction of neurological deficit scores between 40% and 80% are considered effective. No improvement or even deterioration of the clinical symptoms without reduction of neurological deficit scores is considered ineffective (Orgah *et al.*, 2019; Zhang *et al.*, 2019). Overall response rate is equal to those cases of significantly effective and effective are divided by total number multiplied by 100%.

The NIHSS score between the two groups was evaluated and compared (Feng *et al.*, 2019) and a higher score represented a more severe degree of neurological deficit.

Fasting blood glucose data of the two groups were compared, as well as the vascular endothelial function and hemodynamic level.

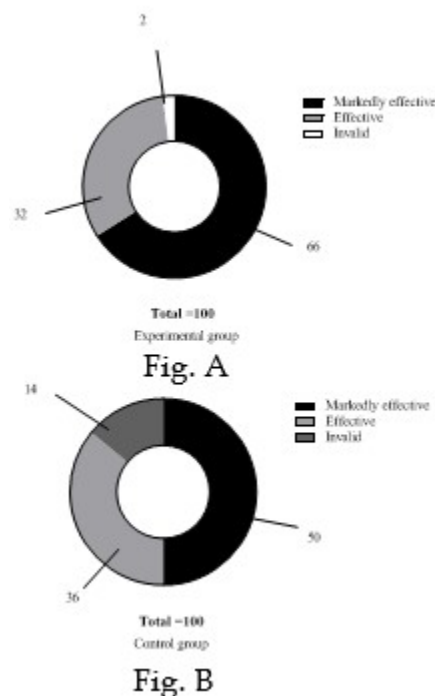
STATISTICAL ANALYSIS

The statistical analysis was conducted using SPSS 20.0 software and image rendering was carried out with GraphPad Prism 7 (GraphPad Software, San Diego, USA). Measurement data were represented as (x ± s) and analyzed using t-test. Count data were represented as (n, %) and analyzed using the chi-square test. P<0.05 indicated a statistically significant difference.

RESULTS

Comparison of general information

There was no significant difference in age, gender, BMI, education level, smoking, drinking, and residence between the two groups (P>0.05), as shown in table 1.



Note: Fig. A represents the expression of therapeutic effect in study group; Fig. B is the expression of therapeutic effect in control group;

In study group, the significantly effective rate was 66.00% (33/50), the effective rate was 32.00% (16/50), the ineffective rate was 2.00% (1/50) and the overall effective rate was 98.00% (49/50).

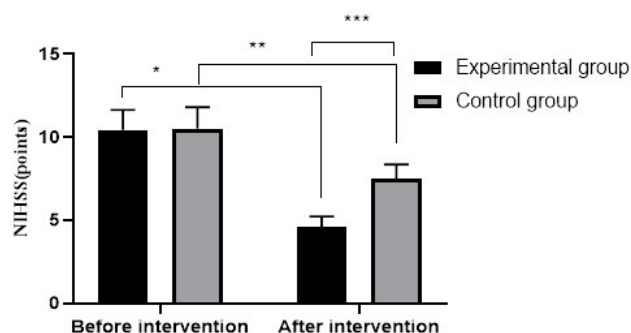
In control group, the significantly effective rate was 50.00% (25/50), the effective rate was 36.00% (18/50), the ineffective rate was 14.00% (7/50) and the overall effective rate was 86.00% (33/50).

There was a significant difference between the two groups ($X^2 = 4.891, P < 0.05$).

Fig. 1: Comparison of therapeutic effect [n (%)]

Comparison of therapeutic effect

The study group obtained an overall response rate of 98.00%, significantly higher than that of 86.00% in the control group ($P < 0.05$), as shown in fig. 1.



Note: Abscissa indicates indexes of before and after intervention, ordinate indicates NIHSS score, points;

The NIHSS scores of study group had (10.44±1.21) points and (4.59±0.64) points, respectively.

In control group, the NIHSS score had (10.51±1.29) points and (7.49±0.87) points, respectively;

*indicated that there was a significant difference in NIHSS score before and after intervention in the study group ($t=30.220$, $P < 0.05$);

**indicated that there was a significant difference in NIHSS score before and after intervention in the control group ($t=13.724$, $P < 0.05$);

***indicated that there was a significant difference in NIHSS score after intervention between the two groups ($t=18.986$, $P < 0.05$).

Fig. 2: Comparison of NIHSS score ($x \pm s$)

Comparison of blood glucose level

There was no significant difference in blood glucose level before treatment between the two groups ($P > 0.05$). Fasting blood glucose level was significantly improved after treatment in both groups compared with the condition before treatment ($P < 0.05$), as shown in table 2.

Comparison of NIHSS score

No significant difference in NIHSS score between the two groups before treatment was observed ($P > 0.05$). After treatment, the NIHSS score in the study group was significantly lower than that in the control group ($P < 0.05$), as shown in fig. 2.

Comparison of vascular endothelial function indicator

After treatment, patients in the study group had significantly better vascular endothelial function indicators than those in the control group ($P < 0.05$), as shown in table 3.

Comparison of incidence of adverse reactions

The incidence of adverse reactions of the two groups was similar ($P > 0.05$), as shown in table 4.

Comparison of hemodynamic indicator

After treatment, there was a significant difference in

hemodynamic indicators between the two groups ($P < 0.05$), as shown in table 5.

DISCUSSION

Cerebral infarction is one of the most common complications among diabetics patients, and the incidence of cerebral infarction is four times higher in diabetics than in non-diabetics. Moreover, diabetics with cerebral infarction mostly experience poor prognoses. Clinical symptoms of diabetes include tiredness, hunger, thirst, sweet urine (Xu *et al.*, 2018). At present, it is believed that the etiological factors of diabetes mellitus complicated with cerebral infarction may be attributed to the excessive oxidation and glycosylation of cerebrovascular endothelial cells, resulting in endothelial cell dysfunction which thus leads to platelet aggregation and thrombosis to impair fibrinolysis. Arterial stenosis may occur after the formation of thrombosis, which ultimately gives rise to cerebral infarction.

According to traditional Chinese medicine, diabetes and cerebral infarction result in the loss of body fluid, phlegm, and disorder of spleen, causing qi stagnation and blood stasis and thus stroke, which underscores the significance of improving blood circulation and promoting qi at meridians (Ravikanth, 2020; Wang *et al.*, 2019). To the best of our knowledge, Danshen, the main component of Danhong injection, may serve as a vasodilator, inhibits platelet aggregation, reduces cerebral ischemia-reperfusion damage and improves poor blood circulation of brain tissue. Moreover, Honghua possesses multiple pharmacological properties, including analgesics, vasodilation, and calcium antagonism. The rich safflower glycosides increase coronary blood flow, dilate the coronary artery, and relieve microcirculatory disturbance. Therefore, Danhong injection has an excellent therapeutic effect on cerebral infarction. Previously this study was conducted on the patient with cerebral infarction. The same injection was evaluated for its effects on patients of cerebral infarction with diabetes (Jiang *et al.*, 2015).

The results showed that Danhong injection could effectively improve the degree of nerve defect among diabetic patients with cerebral infarction. The overall response rate in the study group was up to 98%, significantly better than that in the control group ($P < 0.05$). The incidence of adverse reactions was 2.00% in the study group and 6.00% in the control group, with no significant difference between the two groups ($P > 0.05$). The results are consistent with previous research in which “there was no significant difference on the adverse reaction rate of 1.94% in the study group and 2.37% in the control group ($P > 0.05$)” (Li *et al.*, 2019), suggesting that Danhong injection has a significant therapeutic effect in diabetic patients with cerebral infarction and facilitates rapid recovery.

Table 1: Comparison of general information [n (%)]

	Study group (n = 50)	Control (n = 50)	X2 or t	P
Sex			0.166	0.683
Male	31 (62.00)	29 (58.00)		
Female	19 (38.00)	21 (42.00)		
Age (years)			0.278	0.781
	41.29±3.67	41.08±3.88		
BMI (kg/m2)			0.594	0.553
	26.14±1.67	25.93±1.86		
Education Level				
Primary school or below	15 (30.00)	17 (34.00)	0.183	0.668
Junior high school	19 (38.00)	18 (36.00)	0.042	0.836
High School and Secondary School	9 (18.00)	9 (18.00)	0.000	1.000
College degree or above	7 (14.00)	6 (12.00)	0.088	0.766
Smoking			0.041	0.839
Yes	30 (60.00)	29 (58.00)		
No	20 (40.00)	21 (42.00)		
Alcohol consumption			0.169	0.680

Table 2: Comparison of blood glucose level (X ± S)

Group	N	Before treatment	After Treatment	T	P
Study group	50	7.91±1.08	5.24±0.41	16.343	<0.05
Control group	50	7.87±1.17	6.27±0.44	9.051	<0.05
T		0.178	12.110		
P		> 0.05	< 0.05		

Table 3: Comparison of vascular endothelial function indicator (X ± s)

Group	N	VEGF		VWF (ng/ml)		ET-1 (pg/ml)	
		Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment
Study group	50	179.24±34.48	69.13±5.24	38.84±4.79	11.87±3.54	139.24±22.97	55.97±6.37
Control group	50	176.96±33.97	79.62±6.53	39.13±3.94	14.91±3.41	141.61±24.51	67.91±5.74
T		0.333	8.859	0.331	4.373	0.499	9.846
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

Table 4: Comparison of incidence of adverse reactions [n (%)]

Group	N	Gastrointestinal haemorrhage	Respiratory tract spasm	Anaphylactic shock	Total Occurrence
Study group	50	0 (0.00)	1 (2.00)	0 (0.00)	1 (2.00)
Control group	50	1 (2.00)	1 (2.00)	1 (2.00)	3 (6.00)
X ²					1.042
P					> 0.05

Table 5: Comparison of hemodynamic indicator (X ± s)

Group	N	High shear viscosity		Low shear viscosity		Platelet adhesion		Hematocrit	
		Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment	Before treatment	After Treatment
Study group	50	5.86±0.47	3.01±1.24	13.74±4.17	6.87±1.16	69.71±7.27	49.21±4.51	50.63±4.71	36.71±3.18
Control group	50	5.71±0.56	4.91±1.09	13.91±4.13	9.91±2.37	69.34±7.13	60.12±5.93	50.13±4.07	53.91±4.13
T		1.451	8.138	0.205	8.147	0.257	10.355	0.568	23.333
P		> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05

CONCLUSION

Danhong injection can effectively reduce the symptoms of diabetic patients with cerebral infarction and improve the prognosis, demonstrating that the therapy is safe and effective.

REFERENCES

- Bi C, Li PL, Liao Y, Rao HY, Li PB, Yi J, Wang WY and Su WW (2019). Pharmacodynamic effects of Dan-hong injection in rats with blood stasis syndrome. *Biomed Pharmacother.*, **118**: 109187.
- Cao X, Gong X and Ma X (2019). Diabetic nephropathy versus diabetic retinopathy in a chinese population: a retrospective study. *Med Sci Monit*, **25**: 6446-6453.
- Dai Z, Jiao Y, Fan Q, Qi A, Xiao L and Li J (2020). Homocysteine, interleukin-1 β , and fasting blood glucose levels as prognostic markers for diabetes mellitus complicated with cerebral infarction and correlated with carotid intima-media thickness. *Exp. Ther. Med.*, **19**(2): 1167-1174.
- DeCarlo K and Wallia A (2019). Inpatient management of T2DM and hyperglycemia in older adults. *Curr. Diab Rep.*, **19**(10): 104.
- Feng X, Li Y, Wang Y, Li L, Little PJ, Xu SW and Liu S (2019). Danhong injection in cardiovascular and cerebrovascular diseases: Pharmacological actions, molecular mechanisms and therapeutic potential. *Pharmacol Res*, **139**: 62-75.
- Jiang Y and Lian YJ (2015). Effects of Danhong injection on hemodynamics and the inflammation-related NF- κ B signaling pathway in patients with acute cerebral infarction. *Genet. Mol. Res.*, **14**(4): 16929-16937.
- Kim E, Yang J, Park KW and Cho S (2018). Inhibition of VEGF signaling reduces diabetes-exacerbated brain swelling, but not infarct size, in large cerebral infarction in mice. *Transl. Stroke Res.*, **9**(5): 540-548.
- Li SN, Li P, Liu WH, Shang JJ, Qiu SL, Zhou MX and Liu HX (2019). Danhong injection enhances angiogenesis after myocardial infarction by activating MiR-126/ERK/VEGF pathway. *Biomed Pharmacother.*, **120**: 109538.
- Liu S, Wang K, Duan X, Wu J, Zhang D, Liu X and Zhao Y (2019). Efficacy of Danshen class injection in the Treatment of Acute Cerebral Infarction: A Bayesian network meta-analysis of randomized controlled trials. *Evid Based Complement Alternat Med.*, 5814749.
- Orgah JO, Ren J, Liu X, Orgah EA, Gao XM and Zhu Y (2019). Danhong injection facilitates recovery of post-stroke motion deficit via Parkin-enhanced mitochondrial function. *Restor Neurol Neurosci.*, **37**(4): 375-395.
- Ravikanth R (2020). Relevance of carotid intima-media thickness and plaque morphology in the risk assessment of patients with acute ischemic cerebral infarcts: A case-control study of large series from a single center. *J. Med. Ultrasound.*, **28**(1): 29-34.
- Shi N, He J, Guo Q, Liu T and Han J (2019). Liraglutide protects against diabetes mellitus complicated with focal cerebral ischemic injury by activating mitochondrial ATP-sensitive potassium channels. *Neuroreport.*, **30**(7): 479-484.
- Sreedharan R and Abdelmalak B (2018). Diabetes mellitus: Preoperative concerns and evaluation. *Anesthesiol Clin.*, **36**(4): 581-597.
- Suzuki J, Fuchigami T, Kawamura K, Aoki M, Urakami T and Morioka I (2019). Infantile cerebral infarction caused by severe diabetic ketoacidosis in new-onset type 1 diabetes mellitus. *J. Pediatr Endocrinol Metab.*, **32**(12): 1391-1394.
- Wan H, Huang L, Ge L, Jiang Y, Li G, Leng X, Feng X, Xiang J and Zhang X (2020). Are hemodynamics of irregular small carotid-ophthalmic aneurysms different from those of regular ones and large aneurysms based on numerical simulation? *Neuroradiology*, **62**(4): 511-518.
- Wang Y, Jiang L, Wang XY, Chen W, Shao Y, Chen QK and Lv JL (2019). Evidence of altered brain network centrality in patients with diabetic nephropathy and retinopathy: an fMRI study using a voxel-wise degree centrality approach. *Ther Adv. Endocrinol Metab*, **10**: 2042018819865723.
- Xu W, Zhang Y, Yu Y, Li B, Liu J, Wang P, Wu H, Liu Q, Wei Z, Xiao H and Wang Z (2018). Dose-dependent target diversion of Danhong injection on the Glu-GLT-1/Gly-GlyRa dynamic balance module of cerebral ischemia. *Pharmacol Res*, **135**: 80-88.
- Yuan K, Chen J, Xu P, Zhang X, Gong X, Wu M, Xie Y, Wang H, Xu G and Liu X (2020). A nomogram for predicting stroke recurrence among young adults. *Stroke*, **51**(6): 1865-1867.
- Zhang DQ, Mu YP, Xu Y, Chen JM, Liu P and Liu W (2020). Research progress in Chinese medicine preparations for promoting blood circulation and relieving blood stasis for cirrhotic patients with portal vein thrombosis following splenectomy. *Chin J. Integr. Med.*, Epub ahead of print.
- Zhang Q, Guo J, Dai G, Li J, Zhu L, He S, Zong Y, Tang Z, Zhao B, Ju W and Duan J (2019). Comparison of the pharmacokinetic profiles of ceftriaxone used alone and combined with danhong injection in old rats. *Eur. J. Drug Metab Pharmacokinet.*, **44**(4): 505-517.
- Zhou M, Ren P, Li S, Kang Q, Zhang Y, Liu W, Shang J, Gong Y and Liu H (2019). Danhong injection attenuates high-fat-induced atherosclerosis and macrophage lipid accumulation by regulating the PI3K/AKT insulin pathway. *J. Cardiovasc Pharmacol.*, **74**(2): 152-161.
- Zhu J, Yi X, Zhang Y, Pan Z, Zhong L and Huang P (2019). Systems pharmacology-based approach to comparatively study the independent and synergistic mechanisms of Danhong injection and naoxintong capsule in ischemic stroke treatment. *Evid Based Complement Alternat Med.*, **2019**: 1056708.