Role of traditional Chinese medicine in prevention and treatment of complications after cerebrovascular stent placement*

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Abstract

DBJECTIVE: To evaluate the efficacy of traditional Chinese medicine in the treatment of complications following cerebrovascular stent placement.

METHODS: A computer screen was performed for Science Direct database and Ei database between January 1960 and October 2009, using key words of “traditional Chinese medicine, stent placement, complication”, and the language was limited to English. At the same time, Chinese Journal Full-text database and Chinese Biomedical Literature database between January 1994 and October 2009 were searched for related articles, using key words of “ traditional Chinese medicine, cerebral blood vessels, stent placement, complications’’, and the language was limited to Chinese. In addition, several monographs were manually consulted. The basic and clinical trials addressing the prevention and treatment of traditional Chinese medicine on the complications following cerebrovascular stenting were included.

RESULTS: Subsequent to the cerebrovascular stent placement, the traditional Chinese medicine interventions include benefiting *Qi*, invigorating blood circulation, and eliminating phlegm, which all serve as the basic approach, in addition these interventions are accompanied by relieving *Qi* and stagnancy in liver, soothing the nerves and benefiting water, cooling blood and stopping bleeding. The commonly used traditional Chinese medicine compound is consisted of *Shengmai San*, *Buyang Huanwu decoction*, *Xuefu Zhuyu* decoction, *sini* decoction and resist decoction. Modern pharmacological studies have shown that a large number of traditional Chinese medicine and compound which are always used to benefit *Qi*, invigorate blood circulation, dissipate blood stasis and eliminate phlegm, can effectively prevent the complications following cerebrovascular stent placement through a multi-component, multi-target, multi-channel integration regulatory role.

CONCLUSION: The traditional Chinese medicine interventions during the peri-operative period of cerebral vascular stent placement exhibit a feature of Chinese medicine and play an important role for improving the success rate of surgery, preventing and reducting peri-operative period and long-term complications.

INTRODUCTION

Cerebral vascular stenting has become the major treatment of internal carotid artery and intracranial artery stenosis, but there are still many inevitable complications. Authors believe that both the pathological status of preoperative atherosclerosis, and occurrence of intraoperative, postoperative complications, are characteristics of *Qi* deficiency, blood stasis and phlegm stagnation in terms of pathogenesis. How to arrange the way of traditional Chinese medicine prevention and treatment for its complications? How to improve short-term and long-term efficacy of interventions by applying integrated Chinese and Western medicine treatment, and to exhibit the whole regulation and multi-link combined therapy advantages of Chinese medicine?

MATERIALS AND METHODS

The inclusion and exclusion criteria of literatures

Inclusion criteria: ① cerebral vascular stent placement therapy. ② treatment of complications following cerebral vascular stent placement. ③ application of Chinese medicine in the treatment of cerebral vascular stent therapy.

Exclusion criteria: Meta analysis or repeatable research.

Data extraction strategy

A computer screen was performed for Science Direct database and Ei database between January 1960 and October 2009, using key words of “traditional Chinese medicine, stent placement, complication”, and the language was limited to English. At the same time, Chinese Journal Full-text database and Chinese Biomedical Literature database between January 1994 and October 2009 were searched for related articles, using key words of ”traditional Chinese medicine, cerebral blood vessels, stent placement, complications’’, and the language was limited to Chinese. In addition, several monographs were manually consulted.

Evaluation on the included literatures

The included literatures are regarding the prevention and treatment of complications after cerebrovascular stent placement, and meta-analysis of Chinese medicine application, including basic experimental papers and clinical trials papers.

RESULTS AND DISCUSSION

Results of literature retrieval

A total of 65 relevant literatures were screened out, seven documents of them met the inclusive criteria while 58 documents were excluded for the duplication or Meta analysis. Among seven literatures meeting the inclusion criteria, there are three domestic, while

the rest are foreign research reports.

Results description

Current status of carotid artery and intracranial artery stenosis stenting

A large number of research studies have shown that, intracranial arteries and carotid stenosis are closely related to ischemic cerebrovascular disease, the incidence rate of ipsilateral stroke increases 5%–15% every year[1]. At present, the treatment methods of atherosclerotic stenosis commonly adopt drug therapy, surgery and endovascular treatment. Endovascular interventional therapy includes stent placement, vascular intimal peeling, laser or mechanics-aid vascular recanalization.

Vascular stent is applying balloon to dilate the narrowed blood vessels, and then implanting a permanent mesh metal stent. The stenting on stenotic artery lesion can reduce the disposal of the narrow part of intimal plaque, and improve the narrow-induced brain tissue low perfusion state and prevent the aggravation of stenosis. Compared with the traditional surgical treatment (*e.g.*, endarterectomy), intravascular stent implantation have become a potential treatment of cerebral artery stenosis because of little trauma, without requirement of general anesthesia, and few complications[2]. A large sample, multi-center randomized controlled study of stenting and angioplasty with protection in patients at high risk for endarterectomy show that, artery stenting is equal to endarterectomy short-term (30 days) in reducing the dead rate and ischemic cardiovascular and cerebrovascular event rate in the high-risk surgical population groups; long-term (one year) effects of the treatment is better than endarterectomy[3]. Due to the restrictions of surgical approach, endarterectomy is limited to carotid lesions. The angioplasty and stent implantation can be implemented in the subclavian artery, innominate artery and vertebral-basilar artery system where endarterectomy is difficult to reach, also in the secondary blood vessels such as intracranial artery, middle or posterior cerebral artery. Therefore, the intravascular stent placement has a more broad application prospects in the prevention and treatment of ischemic cerebrovascular disease[4].

Complications and their symptomatic treatment after cerebrovascular stenting

Vascular stent placement, although a minimally invasive surgery, still exhibits some complications, such as cerebral hyperperfusion syndrome, carotid sinus irritation, sinus bradycardia, vascular spasm, hypotension, intimal dissection, aneurysm formation, plaque rupture, plaque hemorrhage, and emboli embolism.

Cerebral hyperperfusion syndrome is seen in patients with severe arterial stenosis and hypertension, due to sudden expansion of arteries, intracranial blood flow may increase significantly, thus causing cerebral hyperperfusion syndrome. In addition, the preoperative, intraoperative and postoperative application of a large number of both anticoagulant and anti-poly drugs, such as intraoperative and postoperative systemic heparin, may result in more complications such as intracranial hemorrhage in patients under the conditions of over-perfusion state of the brain. As for the major symptomatic treatment, you can choose an appropriate dehydrating agent and hormone, then control the blood pressure when dilatation (systolic blood pressure maintained at 100–130 mm Hg), TCD monitoring during the operation is suggested if convenience. Bradycardia and hypotension are caused by stent stimulates the carotid sinus baroreceptor, balloon repeated expansion is more common in patients with severe stenosis with sclerosis plaque, these patients are often engendered by dizziness, severe cases may have a temporary loss of consciousness and even convulsions. The appropriate choice of stent and accurate stent release is a key to prevent the bradycardia and hypotension. During operation (before eluting stent), atropine is used. After the operation, the appropriate application of boosting-pressure drugs and atropine are suggested when bradycardia and hypotension happens.

Vascular spasm is prone to occur under the stimulations of catheter, guide wire and contrast agent, in particular the application of brain protection device. The nimodipine and papaverine are good choices of treatment. Too large diameter of cerebral protection device is not suggested to use. The pre-dilation of stent stenosis before the release of is the best way to prevent stent deformation and displacement, a suitable and accurate stent placement is the key to avoid the complications.

The collapse of cerebral arterial thrombosis atherosclerotic plaque can lead to ischemic stroke. The application of cerebral protection devices can prevent ischemic stroke. CREST showed stroke and mortality were less than 5%, and decreased to less than 2% after the use of cerebral protection device, and most patients have no sequelae. Using the protective umbrella, ischemic stroke can be good prevented.

Mechanism of stent restenosis remains unclear, it may be related to the following factors: vessel recoil, vascular remodeling, and vascular intimal hyperplasia. At present, although with the increasing standards of operating techniques and the applications of corresponding western medicine and methods, some complications can be relieved or even avoided, some complications such as cerebral hyperperfusion syndrome, intracranial hemorrhage following a large number of anticoagulant and anti-poly drugs, postoperative complications such as restenosis, all remain to be resolved, while Chinese medicine can give full advantages of to the overall regulation and multi-link combined therapy, it has attracted more and more attention by the medical profession in terms of the prevention and treatment of vascular complications after stent placement, as well as raising short-term and long-term intervention efficacy in recent years, therefore the authors collated and put forward ideas of Chinese medicine intervention.

Ideas on traditional Chinese medicine to prevent and treat complications after cerebral vascular stent placement

Traditional Chinese medicine thought on the pathological state of atherosclerotic vascular stenosis: Chinese medicine believes that, all diseases of the human body can be analyzed in two aspects. For instance, strong healthy energy is stored in the body, no evil is impossible to offend; and evil has been able to violate the human body, must result from the deficiency of healthy energy, mentioned in the "*Emperor's Canon of Medicine*". During the occurrence and development process of atherosclerosis, a variety of pathological processes have caused arterial damage, including apoptosis, free radical damage and collagen gel in the body's natural aging process.

These damages happen slowly in the body's natural aging process. Therefore, the symptoms shown are relative ease, manifested as deficiency in origin for the atherosclerotic traditional Chinese medicine syndrome, such as the spleen and kidney *Qi* deficiency, the essence emptiness. On the other hand, due to different reasons-caused blood lipids, glucose metabolic disorders, abnormal blood pressure and other factors in human body often damage the arteries, leading to the occurrence of atherosclerosis, and manifested as sputum, blood stasis and other standard pathological damages in traditional Chinese medicine pathogenesis, such as stagnation of phlegm stasis and *Qi* movement stagnation. As two kinds of traditional Chinese medicine pathogenesis, the asthenia in origin and asthenia in superficiality often interact and aggravate the disease, ultimately lead to phlegm and blood stasis in the vein, thus gradually forming atherosclerosis and arterial stenosis. Ideas on traditional Chinese medicine for the complication pathogenesis after cerebral vascular stenting: ① Stent placement can enable blood flow to run smoothly in a short time, play a temporary solution on dispelling stasis, but the organ *Qi* deficiency has still exist. As for its rapid intervention on the stasis, this method is similar to blood breaking in the Chinese medicine, and there are some disadvantages of consumption *Qi* and injuring blood, so after stent placement the organ *Qi* deficiency may also further exacerbated; clinical patients exhibit noticeable weakness and tiredness, lazy words. *Qi* deficiency may induce the weakness in controlling blood, excessive blood breaking of stent implantation, injuring blood and consummating *Qi*, as well as natural weak essence, it is more prone to occur over-perfusion syndromes, such as bloody pupil and intracranial hemorrhage. ② Artery stenosis lesion has already exhibited heavy phlegm and blood stasis, during stent implantation process, the mechanical stimulation may lead to aggravate the local air-block, thereby affecting the operation of the blood and body fluid, water blocking induces edema and muddy phlegm, blood stagnation induces blood stasis, so intimal injury and inflammation edema may appear during operation; severe phlegm may form partial occlusion of blood vessels, namely, thrombosis; or after stent expansion, local phlegm and blood stasis may dispel, but does not dissipate, this lesion can flow to the remote, to obstruct distal vessels, to form vascular occlusion, namely emboli shed, and to form a variety of ischemic stroke. ③ Intraoperative catheter or stent stimulation of the arteries and veins, it will inevitably disrupt the local blood running, moreover, the emotional stress of patients during surgery can also cause the liver failing to maintain the normal flow of *Qi*, poor general *Qi* and activity, thereby increasing the local blood running disorder, leading to localized blood contracture, and forming blood vessel spasm. ④ From a Chinese medical point of view, vascular stent implantation is a treatment of exogenous trauma, postoperative restenosis is a kind of Stasis Syndrome. It is this exogenous trauma, combined with stenting-induced the injured blood and consumption *Qi*, health energy deficiency in human body, that leads to the second interaction of the phlegm and blood stasis that has already cleared, forming a postoperative restenosis.

Ideas on traditional Chinese medicine for cerebral vascular stent placement

Benefiting *Qi*, activating blood and dispelling phlegm are the main treatment principles for the complications following stent placement: prior to stent placement, the asthenia in superficiality syndrome is predominant and asthenia in origin is secondary, the corresponding treatment should include promotion method of activating blood, eliminating sputum and promoting blood circulation, in combination with nutrition method of benefit *Qi* and improve yang; after stent placement, asthenia in origin syndrome is predominant and asthenia in superficiality is secondary, the corresponding treatment should include nutrition method in combination with promotion method. As a means of palliative treatment, although interventional therapy can solve the asthenia in superficiality, the asthenia in origin still exist following interventional treatment, moreover the intervention itself, as an exogenous injury, has caused a new blood stasis, so no matter whether complications appear after intervention, *Qi* deficiency and phlegm stasis are the basic pathological basis before and after intervention. Therefore, benefiting *Qi*, activating blood and eliminating phlegm are primary treatment rules for the complications following angioplasty and stent implantation, in addition, some methods can also be accompanied, such as promoting *Qi*, calming nerves, benefiting water, cooling blood, and stopping bleeding, so as to prevent intraoperative and postoperative complications, to improve patient quality of life after interventional therapy. Choice of traditional Chinese medicine to treat complications after cerebrovascular stenting: Chinese medicine intervention after stent placement includes benefiting *Qi*, promoting blood circulation, eliminating phlegm, serving as the basic principles, which can be accompanied by dispersing the depressed liver-energy, regulating vital energy, calming nerves, benefiting water, cooling blood and stopping bleeding. According to the author's clinical experience, the commonly used drugs for benefiting *Qi* are mainly Milkvetch Root, Tangshen, Common Yan Rhizome, *etc*.; promoting blood circulation drugs are mainly Szechwan Lovage Rhizome, Red Peony Root, Danshen Root, Motherwort Herb, Sanchi, Lalang Grass Rhizome, Cattail Pollen, *etc*. Among them, Motherwort Herb, Sanchi, Lalang Grass Rhizome, Cattail Pollen could activate blood circulation, stop bleeding, benefit water and alleviate edema; eliminating phlegm drugs are mainly Arisaema with Bile, Thunberg Fritillary Bulb, Seaweed, *etc*. Drugs for regulating *Qi* are mainly Turmeric Root Tuber and Yanhusuo, which both can regulate *Qi* and promote blood circulation. The commonly used traditional Chinese medicine compound includes *Shengmaisan*, *BYHWD*, *Xuefuzhuyu* decoction, *Sini* decoction, and resist decoction. Modern pharmacological studies have shown that a large number of Chinese medicine compound for benefiting *Qi*, activating blood, dissipating blood stasis and eliminating phlegm can effectively intervene the incidence of complications after stent placement through the multi-component, multi-target, multi-channel integration and regulatory role. Single Chinese medicine and its extract: Astragalus and so on have become a popular and effective traditional Chinese medicine, and have been widespread reported: Astragalus has a variety of pharmacological effects on cerebral blood vessel, it can inhibit platelet aggregation, reduce blood viscosity and coagulation degree, enhance plasmin activity, relax smooth muscle, expand brain blood vessels, reduce vascular resistance, improve blood circulation especially microcirculation, inhibit the formation of arterial thrombosis, reduce lipid peroxidation, reduce malonyl

aldehyde generation, scavenge free radicals, and decrease the damage caused by ischemia-reperfusion; *Danshen* can inhibit vascular smooth muscle cell proliferation in a dose-dependent manner, also has calcium antagonistic effects, can affect platelet aggregation, prevent and treat restenosis as an effective traditional Chinese medicine. Fixed prescriptions: ① *BYHWD*: Decoction is the classic Chinese medicine prescription of benefiting *Qi*, activating blood circulation, and eliminating stasis, the experimental studies have shown that BYHWD has some regulatory role on PDGF receptor mRNA of vascular endothelial damage, it can increased significantly aortic smooth muscle cells SOD-l gene expression, inhibit the PDGF receptor mRNA expression in the leading edge of vascular endothelial intima area, the above mechanisms could protect cell membrane and reduce the pathological proliferation of blood vessel walls, thereby preventing the restenosis[5]. ② *Xuefuzhuyu decoction*: *Xuefuzhuyu decoction* is the classic prescription of activating blood circulation and eliminating stasis, the experimental studies have shown that it has a lipid-lowering effect, inhibit platelet adhesion and aggregation, anti-arteriosclerosis, reduce the restenosis rate of rabbit iliac artery by the percutaneous transluminal angioplasty, and inhibit vascular smooth muscle cell proliferation, the latter mechanism is the inhibition of vascular smooth muscle cells DNA synthesis, reduction of vessel wall PDGF-R, oncogene c-myc mRNA expression level and ET levels, increase CGRP and so on, have a positive effect on the prevention and treatment of intraoperative and post-operative complications[6]. ③ Modified resist decoction: As a response to the mechanism of postoperative complications taking blood stasis as a superficiality, while organ *Qi* weakness, particularly the liver *Qi* deficiency and adverse conveyance and dispersion as an origin, Wu *et al*[7] added leech, cooked rhubarb, cinnamon to the resist decoction, results showed that this decoction could effectively reduce serum triglycerides and low-density lipoprotein apolipoprotein content, improve the high density lipoprotein apolipoprotein content, reduce the rate of platelet adhesion and aggregation, increase SOD activity and NO levels, reduce malondialdehyde content and endothelin concentration, in order to protect vascular endothelium, to help vasomotor function, and to inhibit the expression of proliferating cell nuclear antigen in vascular smooth muscle cells. These may be the important mechanisms underlying anti-stent restenosis.

This study was aimed to primarily explore the traditional Chinese medicine interventions for cerebral vascular stent placement during the perioperative period, to play a feature of traditional Chinese medicine, and is of great significance for improving the success rate of surgery, preventing and reducing perioperative and long-term complications.

REFERENCES

[1] Branett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med. 1998;339(20):1415-1425.

[2] Phatoums CC, Higashida RT, Malek AM, et al. Carotid artery stentp lacement for athemsclemtic disease: rationale, technique, and current status. Radioloy. 2000;217(1):26-41.

[3] Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med. 2004;351(15):1493-1501.

[4] Alhaddad IA. Carotid artery surgery vs. stent: A cardiovascular perspective. Catheter Cardiovasc Interv. 2004;63(3):377-384.

[5] Yu B, Chen KY, Mao JM, et al. Xuefuzhuyu pills 43 cases of coronary heart disease prevention and treatment of coronary stent restenosis after implantation of clinical research. Zhongguo Zhongxiyi Jiehe Zazhi. 1998;18(10):585.

[6] Xie QJ, Wu WK, He Q, et al. Bu Yang Huan Wu Tang right hit vascular endothelial PDGF receptor gene expression in vitro. Zhongyiyao Xinxi. 1997;1(1):40.

[7] Wu WK, Huang HQ, Wang QH, et al. Tang betterment to withstand anti-rabbit experimental study of restenosis after PTCA. Zhongguo Zhongyiyao Keji. 2001;8(5)285.

中医药在脑血管支架置入后防治并发症中的作用*

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摘要

目的：评价中医药在脑血管支架置入后并发症中的作用效果。

方法：应用计算机检索 Science Direct 数据库、Ei 数据库 1960-01/2009-10 期间的相关文章，检索词为“traditional Chinese medicine，stent placement，complication”，并限定文章语言种类为 English。同时计算机检索中国期刊全文数据库、中国生物医学文献数据库等 1994-01/2009-10 期间的相关文章，检索词为“中医药，脑血管，支架置入，并发症”，并限定文章语言种类为中文。此外还手工查阅相关专著数部。纳入有关中医药防治脑血管支架置入后并发症的基础与临床实验。

结果：脑血管支架置入后的中医药干预方法以益气、活血、涤痰为基本治法,亦可佐以疏肝理气、安神利水、凉血止血之品。常用的中药复方有生脉散、补阳还五汤、血府逐瘀汤加减、四逆汤及抵挡汤加减等。现代药理学研究表明，大量益气活血化瘀涤痰的中药及复方，通过多组分、多靶点、多途径的整合调节作用，有效地干预脑血管支架置入后并发症的发生。

结论：对脑血管支架置入围手术期进行中医药干预，发挥中医药特色，对于提高手术成功率，防治、减少围手术期及远期并发症具有重要意义。

关键词：脑血管；支架置入；中医药；医学植入物；并发症

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