

Review Article

Remote Ischemic Conditioning: A Novel Non-Invasive Approach for Secondary Prevention of Middle Cerebral Artery Occlusion Stroke

Zichen Tian¹ and Jing Zhang²

¹ Carleton College, Northfield, Minnesota 55057, USA and

² Department of Neurology, Xuanwu Hospital, Capital Medical University, Beijing, 100053, PRC

Intracranial atherosclerotic stroke is a common type of stroke with a high annual recurrence rate (18.8%). Among them, middle cerebral artery occlusion therapy is still limited, and secondary prevention is far from satisfaction. Because the insufficient cerebral perfusion due to occlusion of blood vessels is the basis of stroke recurrence, improving cerebral perfusion has become the key to secondary prevention of this type of stroke. Remote ischemic conditioning (RIC) is a non-invasive and easy-to-use physical strategy that can be used to protect essential organs such as the brain, heart and kidney. Results of previous clinical studies show that long-term application of RIC can be used as an effective secondary prevention through improving cerebral perfusion with non-occlusive symptomatic intracranial atherosclerosis stenosis (ICAS) and reducing stroke recurrence. Thus, RIC could be widely used as a promising secondary prevention measure in clinical practice to prevent symptomatic middle cerebral artery occlusion and reduce the risk of stroke recurrence.

Key words: intracranial atherosclerotic stroke, remote ischemic conditioning

Introduction

Remote ischemic conditioning (RIC) is a protective systemic strategy by which one or more cycles of brief and nonlethal limb ischemia confer protection to distant organs. It has been proven to be an effective strategy for cardio-protection in patients with ischemic cardiovascular diseases, and it is also effective for neuroprotection in patients with hemorrhagic stroke, acute ischemic stroke and chronic cerebral ischemia (5, 8, 16). In recent years, through clinical trials, it has been verified for the first time that

long-term application of RIC can reduce stroke recurrence in patients with non-occlusive symptomatic intracranial atherosclerosis stenosis (ICAS). It is an effective secondary prevention (12), and is suitable in elderly patients (>80 years old) (13). Moreover, it has been proved to reduce the incidence of stroke in patients with severe internal carotid artery stenosis and to improve the safety of surgery (20). RIC has also showed the benefits in cerebral small vessel disease by improving cerebral blood flow, reducing white matter damage, improving cerebral perfusion and improving cognitive impairment (14). Only minor adverse effect has been showed in these studies (5, 8, 11, 12, 13, 14, 16, 20). There is no evidence of its use in patients with symptomatic occlusive ICAS (middle cerebral artery occlusion) stroke. Based on the promising neuroprotection functions of RIC, we expect that RIC may prevent symptomatic middle cerebral artery occlusion stroke and reduce the risk of stroke recurrence.

ICAS

ICAS has a high incidence in China as one of leading causes of fatal and disabling strokes (50%) (1, 2, 4). Insufficient cerebral perfusion due to arterial stenosis and/or occlusion is the basis for the onset and/or recurrence of stroke (an annual recurrence rate of 18.8%) (3, 6, 7, 19). In secondary prevention measures, in addition to antiplatelet aggregation and the use of statins, some patients can be assisted with stent implantation and extracranial-intracranial artery bypass surgery (17, 18, #1). However, as a subtype of ICAS, patients with acute middle cerebral artery occlusion have no effective strategy as secondary

Corresponding author: Dr. Jing Zhang, Department of Neurology, Xuanwu Hospital, Capital Medical University, Beijing, PRC. Email: zhangjing0909@163.com

Received: December 20, 2019; Revised: January 24, 2020; Accepted: January 26, 2020.

#1 Journal of Chinese Neurology 51: 666-382, 2018.

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prevention. The benefits of arteriovenous thrombolysis, endovascular thrombectomy and extracranial-intracranial artery bypass surgery are easily offset by perioperative complications (7, 15, #1, #2). In addition to the limited treatment options, middle cerebral artery occlusion can lead to hypoperfusion of the brain, which affects prognosis and promotes stroke recurrence. Therefore, it is not conducive to secondary prevention (9, 10). Relapses increase disability and place a huge burden on patients and the national economy (4, 7, 19).

Compensative improvement of cerebral perfusion is the most important way to promote stroke recovery and secondary prevention (9, 10). Therefore, the development of new treatment may be a potentially effective secondary prevention method for middle cerebral artery stenosis patients.

RIC Application in ICAS

RIC has been widely used in clinical trials to test its protective effect on different organs including brain, heart and kidney. Based on the evidence from current clinical studies, RIC can effectively improve cerebral perfusion, protect the brain and prevent recurrence of stroke, especially in patients with non-occlusive ICAS. Results of previous studies have shown that long-term application of RIC can improve cerebral perfusion in patients with non-occlusive symptomatic ICAS (90 days: 36.1% vs. 6.7%, 300 days: 76.3% vs. 53.3%), and reduce stroke recurrence (90 days: 5% vs. 23.3%, 300 days: 7.9% vs. 26.7%). This is a clear evidence that RIC is effective and safe to be used as the strategy of secondary prevention. At the same time, the study suggested that RIC improved the neurological recovery rate (mRS ≤ 1) for 3 months in patients with symptomatic ICAS (90 days: 65.8% vs. 13.3%) without adverse reactions (12). At present, this technology is known internationally as “the promising treatment method for ICAS” (7). Therefore, we assume that RIC is also applicable to patients with symptomatic middle cerebral artery occlusion stroke and is a potential and effective secondary prevention method.

Perspective

RIC could be supported by the evidence from previous clinical trials on the efficacy secondary prevention on non-occlusive symptomatic ICAS patients, as well as proved cerebral protective effect in other types of stroke patients. RIC-based clinical studies have verified its safety and compliance. However,

it is needed to verify the validity of RIC through clinical trials. In the future, we will plan to recruit patients with symptomatic middle cerebral artery occlusion stroke as observation subjects and the RIC will be performed on patients twice daily for 12 months. Moreover, we will plan to conduct randomized controlled trial to verify the effectiveness of secondary prevention through cerebral perfusion levels, stroke recurrence, side effects and stroke prognosis. If it is verified by the proposed clinical trial, RIC can be widely used as a promising secondary prevention strategy for the patients with symptomatic middle cerebral artery occlusion and the recurrence of stroke, and may bring them health and hope.

Conclusion

For patients with symptomatic middle cerebral artery occlusion stroke, RIC may be a potential and effective secondary prevention method. The application of RIC can improve cerebral perfusion, reduce stroke recurrence and improve stroke prognosis. If the above hypothesis can be verified through clinical trials, RIC is widely used as a non-invasive and low-cost adjuvant therapy in patients with symptomatic middle cerebral artery occlusion.

Acknowledgments

This work was supported by The Beijing Municipal Administration of Hospitals Incubating Program, Code: PX2018033.

Conflict of Interest

The authors declare that there is no conflict of interest.

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