Effect and Molecular Mechanism of Physiological Ischemia Training of Skeletal Muscle on Angiogenesis at Remote Sites with Pathological Ischemia in Rabbit Models of Coronary and Peripheral Artery Stenosis

JIANAN LI, MEI SHEN, JING GAO

From Nanjing Medical University, Nanjing, China

Background

This study was designed to test the hypothesis that physiological ischemia exercise training of normal limb can promote angiogenesis in pathological ischemic limb.

Method

The New Zealand white rabbits had left femoral artery ligated (FAL) and electrode implantation performed on the right sciatic nerve. They were randomly assigned to 4 groups. FAL-N was the group without electrical stimulation (ES). FAL-HE had its subjects with high intensity ES (2.5 mA, 40 Hz, 1 ms) on the right hindlimb. FAL-LE had its subjects with low intensity ES (0.3 mA, 40 Hz, 1 ms) on the right hindlimb. BFAO-HE had its subjects with FAL on both hindlimbs and high intensity ES (2.5 mA, 40Hz, 1 ms) on the right hindlimb. The ES procedure was 5 minutes stimulation followed by 5 minutes rest, repeated 8 times daily for 4 weeks. Collateral circulation was grossly examined by angiography, relative blood flow was measured by microspheres technique. Collateralization was evaluated by immunohistochemistry. VEGF mRNA and protein detection were analyzed by western blot and real time RT-PCR.

Results

Collateral blood flow in all major muscles of the left hind limb in the FAO-HE was the highest among the 4 groups ($P<0.01$). Capillary supply ($P<0.001$), expression of VEGF mRNA ($P<0.001$) and protein ($P<0.01$) in gastrocnemius muscle remarkable increased in FAO-HE, there was no statistically significant difference among other groups.

Conclusion

Angiogenesis associated with up-regulation of VEGF expression in the pathological ischemic limb may be facilitated by the physiological ischemic exercise training with normal limb for 4 weeks.

Address for reprints: Prof. Jianan Li
Nanjing Medical University, Nanjing, China

Received October 8, 2008; accepted October 29, 2008