論 文 要 旨

Protective effects of recombinant human soluble thrombomodulin on ischemia reperfusion injury of the spinal cord in rabbits

遺伝子組み換えトロンボモジュリンの虚血再灌流障害に対する脊髄保護効果

今釜 逸美

Abstract

OBJECTIVES: Paraplegia is a well-known severe complication of ischemic spinal injury that occurs during surgery for descending thoracic and thoracoabdominal aortic aneurysm. Although several surgical procedures and medications have been used to prevent paraplegia, the strategy for preventing paraplegia has not yet been established. Thrombomodulin (TM), expressed on the plasma membrane of endothelial cells, has been considered to exert cytoprotective effects against ischemia reperfusion injury (IRI). The protective effect of recombinant human soluble (rhs) TM against IRI in the liver and kidneys has been reported; we investigated whether rhsTM can prevent paraplegia in a rabbit ischemic spinal injury model. Moreover, we examined whether rhsTM protects rat pheochromocytoma cell line, PC12, from hypoxia-reoxygenation damage.

METHODS: Twenty-two New Zealand white rabbits were intravenously injected with isotonic saline (group C; n = 11) or isotonic saline containing rhsTM (group T; n = 11) before clamping of the aorta just below the branching of the renal artery for 30 minutes. Hind limb motor function was assessed 48 hours after aortic declamping as per the modified Tarlov score. PC12 cells were pretreated without rhsTM (group N) or with 1 μg or 10 μg of rhsTM (group A1 or A2), oxygen and glucose were depleted for 210 minutes, and the cells were incubated for another 24 hours. The

cell viability was assessed using the Methyl thiazolyl tetrazolium (MTT) method.

RESULTS: Lower limb motor function was significantly better in group T as compared to that in group C *in vivo* experiment ($p < 0.05$). The cell viability of the PC12 cells in group A2 was higher than that in group N after the hypoxia-reoxygenation experiment ($p < 0.05$).

CONCLUSIONS: The results suggest that rhsTM may prevent paraplegia due to IRI of the spinal cord during surgical intervention for descending thoracic and thoracoabdominal aortic aneurysm.

Keywords: descending thoracic and thoracoabdominal aortic aneurysm, ischemia reperfusion injury, spinal cord, recombinant human soluble thrombomodulin

（ Medical journal of Kagoshima University IN PRESS ）