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Saiko-ka-Ryukotsu-Borei-to inhibits intimal thickening in carotid artery after balloon injury in cholesterol-fed rats

○Hwa-Jin Chung[1], Ikuro Maruyama[2], Tadato Tani[1]

Institute of Natural Medicine, Toyama Medical and Pharmaceutical University[1], School of Medicine, Kagoshima University[2]

Objectives: We have reported the inhibitory effect of Saiko-ka-Ryukotsu-Borei-to (SRB) on intimal thickening and vascular smooth muscle cells (VSMCs) proliferation in carotid artery after balloon injury in rats fed on a normal diet[1]. Since hypercholesterolemia is one of the risk factors of atherosclerosis, we assessed the inhibitory effect of SRB in cholesterol-fed rats.

Methods: Balloon injury of the rat carotid artery was performed according to our previous method[1]. Rats were fed on diet containing 1% cholesterol and SRB extract (3 doses) for 3 days before and 7 days after denudation. Simvastatin (SV) was used as a positive control. 1) Intimal thickening: From the observation in the carotid artery sections, stenosis ratio (%) is calculated from (intimal area) x 100 / (intimal area + luminal area). 2) VSMCs proliferation: By immuno-histochemical method, proliferating cell nuclear antigen (PCNA)-labeling index (%) is calculated from (PCNA positive VSMCs) x 100 / (total VSMCs). 3) Serum and liver lipids: The total cholesterol, TG, HDL-C, LDL-C and lipid peroxides were determined.

Results & Discussion: SRB dose-dependently suppressed the stenosis ratio and PCNA labeling index after balloon endothelial denudation. At 10 times equivalent to human dose, the inhibitory effects of SRB (750 mg/kg/day) on intimal thickening and VSMCs proliferation tended to be greater ($p<0.1$) than those of SV. Although both drugs suppressed lipid levels in serum and liver, SRB was weaker than SV. Thus the inhibitory effects of SRB on the intimal thickening by depending on suppressing VSMCs proliferation. These results suggest the potential for using SRB as a clinical therapeutic strategy in atherosclerosis prevention. The cellular and molecular mechanism of the effects of SRB on migration and cell-cycle of VSMCs are in progress.

1) Kim D-W., et al.: J. Pharm. Pharmacol., 54, 571-575, 2002.