Abnormal proliferation of vascular smooth muscle cells (VSMCs) play an important role in the pathogenesis of hypertension and restenosis induced by balloon injury. Recently, interferon (IFN) was shown to be a selective inhibitor of collagen gene expression in fibroblasts. p27 is a cyclin-dependent kinase inhibitor protein, can limit the vascular proliferation in response to artery injury. The present study aims to investigate the effect of IFN-gamma VSMC growth in vitro and vivo. Culture rat aortic VSMC and rabbit iliac artery were used in present study. Proliferative cell nuclear antigen (PCNA) and p27 were evaluated by Western blot. IFN-gamma (500 u/ml) significantly inhibited 100 nmol/L angiotension II (Ang II) induced PCNA up-regulation in VSMC [PCNA expression (OD value): Control, 75+/−/−; IFN-gamma, 57+/−/−; Ang II, 123+/−/−; Ang II+IFN-gamma, 98+/−/−, P<0.05]. VSMC was incubated by IFN-gamma (500 u/ml) for 24 hrs. p27 protein expression of VSMC was markedly enhanced by IFN-gamma (p 27 (OD value): 210+/−/− vs 237+/−/−, p<0.01). In vivo study, rabbit iliac artery was injured by balloon. PCNA expression of iliac artery was significantly increased after operation at third day. Injection of IFN-gamma (100000 u/kg/day) for three days can markedly depressed the PCNA expression of rabbit iliac artery (OD value: control, 111+/−/− vs 216+/−/−, p<0.01). The present study established the feasibility of IFN-gamma application as a novel approach to improve vascular remodeling and dysfunction in the pathogenesis of hypertension and restenosis by coronary angioplasty.

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Key Words: Vascular Smooth Muscle Cell, Interferon-Gamma, Growth

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INCREASING PLATELET-DERIVED GROWTH FACTOR RECEPTOR-ALPHA MEDIATED THE GROWTH OF VASCULAR SMOOTH MUSCLE CELLS IN SPONTANEOUSLY HYPERTENSIVE RATS
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Previous studies demonstrated that increase of platelet-derived growth factor AA (PDGF-AA) expression correlates with high blood pressure and remodeling of arteries from renal hypertensive rats. PDGF-AA binding its receptors (PDGFR-alpha/beta) leads to either vascular smooth muscle cells (VSMCs) proliferation or vasconstriction. It was unclear which PDGFR subtypes contribute to this process and how PDGF-AA and PDGFR plays their roles in proliferation and hypertrophy of vascular smooth muscle cells (VSMC) in spontaneously hypertensive rat (SHR). Aortic VSMC was isolated from aorta from both rats and cultured. Expression of PDGF-AA, PDGFR-alpha / beta in VSMC of SHR and WKY were observed by Western blot. Proliferation and hypertension of VSMC was observed by measurement of proliferative cell nuclear antigen (PCNA) and 3H-TdR and 3H-Leu incorporation. PDGF-AA and PDGFR-alpha expression in VSMC were markedly increased in than WKY, but PDGF-beta expression was not different between SHR and WKY. Administration of PDGF-AA (20 ng/ml) significantly increased the PCNA expression of VSMC of SHR compared with WKY [WKY, 8.9+/−/− 0.21 vs SHR, 22.5+/−/− 0.27, P<0.01]. PDGF-AA dose-dependently increased PCNA expression of VSMC in SHR, but this effect was not found in WKY. Similarly, PDGF-AA dose-dependently increased the 3H-TdR and 3H-Leu incorporation in VSMC of SHR. PDGF-AA only had a weak effect on 3H-TdR and 3H-Leu incorporation in VSMC of WKY. It concluded that increasing of PDGF-AA and PDGFR-alpha expression in SHR may be responsible for abnormal vascular growth in pathogenesis of primary hypertension. Antagonizing PDGFR-alpha may be a new target for preventing vascular remodeling and restenosis.

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Key Words: Spontaneously Hypertensive Rat, Platelet-Derived Growth Factor Receptor, Vascular Smooth Muscle Cell