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# EFFECTS OF ENALAPRIL AND IRBESARTAN ON CAROTID ARTERY REMODELLING AND TGF- $\beta$ 1/SMADS PATHWAY IN RENOVASCULAR HYPERTENSIVE RATS

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Qian-Hui Shang, Jian-Ling Chen, Wei Hu, Chan Liu, Wan-Heng Mao, Qian-Hui Shang.  
*Institute of Clinical Medicine, Department of cardiology of Affiliated Hospital, Zunyi Medical College, Zunyi Guizhou 563003, China*

**Objectives** To investigate the effects of single-drug or combination therapy of enalapril and irbesartan on carotid artery remodelling and TGF- $\beta$ 1/Smads signal pathway.

**Methods** Renovascular hypertensive rats (RHR) developed by 'two-kidney and one-clip' method were treated respectively with distilled water (model group, n=6), enalapril (10 mg/(kg d), n=6), irbesartan (50 mg/(kg/d), n=6) and enalapril plus irbesartan (5 mg/kg/d+25 mg/(kg d), n=6) for 6 weeks. Six sham-operated rats were used as controls. Carotid artery morphology and structural changes were observed through HE staining, immunohistochemical staining and Masson staining. Media thickness (MT), lumen diameter (LD), media thickness and lumen diameter ratio (MT/LD) and collagen fibre area percentage of carotid arteries were measured. Moreover, the immunohistochemical staining was applied to detect the expression of alpha-smooth muscle actin ( $\alpha$ -SMA), proliferating cell nuclear antigen (PCNA), TGF- $\beta$ 1, p-Smad2/3 and Smad7.

**Results** In the model group, the media thickness was significantly increased, and the volume of vascular smooth muscle cell (VSMC) increased and disarranged. MT, LD, MT/LD,  $\alpha$ -SMA, PCNA and collagen fibre area percentage of carotid arteries in the model group were higher than those in the sham-operated group ( $p<0.01$ ), and TGF- $\beta$ 1 and p-smad2/3 were increased whereas Smad7 was decreased in the model group ( $p<0.01$ ). Single enalapril or irbesartan therapy decreased MT, MT/LD and the protein expression of TGF- $\beta$ 1, p-Smad2/3, and increased the expression of Smad7. Combined enalapril and irbesartan treatment showed significant reductions in above experimental indices than single drug interventions (all  $p<0.05$ ).

**Conclusions** The TGF $\beta$ 1/Smads signalling pathway may be involved in carotid remodelling of RHR. Enalapril or irbesartan can attenuate carotid remodelling of RHR through regulating TGF- $\beta$ 1/Smads pathway and both combination treatment seems to have interaction.