Inhibitory roll of nitric oxide (NO)-containing nerves in adrenergic neurotransmission is decreased in mesenteric resistance arteries of 2-kidey 1-clip hypertensive rats

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We have demonstrated innervation of nitric oxide (NO)-containing nerves (NO nerve) in rat mesenteric arteries and inhibitory roll of NO nerves in perivascular adrenergic neurotransmission. Adrenergic vasoconstrictor function has been shown to increase in hypertension. Therefore, to investigate roll of NO nerves in adrenergic neurotransmission in hypertension, we studied changes in function of adrenergic nerves and NO nerves and interaction between adrenergic nerves and NO nerves. As a hypertensive model, 2-kidney, 1-clip renal hypertensive rats (2K-1C RHR) were used in this study. Under ether anesthesia, 6 week-old Wistar male rat was subjected to clip the left renal artery with a silver ribbon (0.2 mm slit width). Control rats were sham-operated without clipping. 4 weeks after the surgery, 2K-1C RHR and control rats were anesthetized and the mesenteric vascular bed was isolated to prepare for perfusion. After the endothelium was removed, vasoconstrictor responses to periarterial nerve stimulation (PNS) and norepinephrine (NE) injection were observed, and the effect of L-NAME, nonselective NO synthase (NOS) inhibitor, on adrenergic nerve mediated vasoconstriction were studied. In preparations from 2K-1C RHR, vasoconstrictions induced by PNS and NE injection were significantly greater than those in preparations from Control. L-NAME augmented the vasoconstriction induced by PNS but not NE injection in both 2K-1C RHR and Control. However, the facilitatory effect of L-NAME in 2K-1C RHR preparations was smaller than that in Control preparations. Western blot analysis of neuronal NOS (nNOS) in mesenteric arteries from 2K-1C RHR showed significantly smaller expression compared with Control arteries. Immunostaining of the mesenteric arteries showed the presence of nNOS-like immunopositive nerve fivers, which were decreased in 2K-1C RHR compared with sham-operated rat. These results suggest that NO nerves inhibit the adrenergic neurotransmission, and its inhibitory function is decreased in 2K-1C RHR. These altered perivascular nervous systems lead to increase vascular resistances and develop and maintain the hypertension.