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Inhibition of HIF-1 α Alleviates Exaggerated Pressor Response Induced by Static Muscle Contraction in Rats with Peripheral Arterial Disease

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Objective Hypoxia-inducible factor 1 α (HIF-1 α) is a transcription factor mediating adaptive responses to hypoxia and ischemia. A prior work showed that HIF-1 α is increased in sensory nerves of rats with femoral artery occlusion. The present study was to examine if the reflex response of blood pressure induced by muscle contraction was altered after injection of HIF-1 α inhibitor BAY 87-2243 (BAY87) into the arterial blood supply of the ischemic hindlimb muscles.

Methods A rat model of femoral artery ligation was used to study peripheral artery disease. Western blot analysis was employed to examine the protein levels of HIF-1 α in the dorsal root ganglion (DRG) tissues. The exercise pressor reflex was evoked by static muscle contraction.

Results HIF-1 α was increased in the DRG of occluded limbs (optical density: 0.89 ± 0.13 in control vs. 1.5 ± 0.05 in occlusion; $P < 0.05$, $n=6$ in each group). Arterial injection of BAY87 (0.2 mg/kg) inhibited expression of HIF-1 α in the DRG of occluded limbs three hours following its injection (optical density: 1.02 ± 0.09 in occluded limbs with BAY87 vs. 1.06 ± 0.1 in control limbs; $P > 0.05$, $n=5$ in each group). In addition, muscle contraction evoked a greater increase in blood pressure in occluded rats. BAY87 attenuated the enhanced pressor response in occluded rats to a greater degree than in control rats.

Conclusions Inhibition of HIF-1 α alleviates exaggeration of the exercise pressor reflex in rats under ischemic circumstances of the hindlimbs induced by femoral artery occlusion.