Arginase-endothelial nitric oxide synthase imbalance contributes to endothelial dysfunction during chronic intermittent hypoxia

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OBJECTIVE:: Chronic intermittent hypoxia (CIH), the main feature of obstructive sleep apnoea, is associated with impaired vascular function despite unaltered response to nitric oxide donors. This study addressed whether arginase contributes to the endothelial dysfunction in CIH rats. METHODS:: Adult male Sprague-Dawley rats were exposed for 21 days to CIH (5% oxygen, 12 times/h, 8h/day). The internal carotid arteries were isolated to study endothelial nitric oxide synthase (eNOS) and arginase-1 levels by western blot and immunohistochemistry, and their vasoactive responses using wire myography. Relaxation to sodium nitroprusside (SNP; nitric oxide donor) in the presence or absence of soluble guanylyl cyclase inhibitor, and acetylcholine with and without a NOS inhibitor [N-nitro-L-arginine (L-NA)] and the arginase inhibitor BEC were determined. RESULTS:: Arteries from the CIH rats presented higher active contraction induced by KCl (3.5±0.4 vs. 2.3±0.2N/m), augmented media-to-lumen ratio (?40%), decreased relaxation to acetylcholine (12.8±1.5 vs. 30.5±4.6%) and increased sensitivity to SNP (pD2 7.3±0.1 vs. 6.7±0.1). Arginase inhibition reversed the impaired acetylcholine-induced relaxation in CIH arteries (49.5±7.4%), an effect completely blocked by L-NA. In the carotid arteries, arginase-1 protein level was increased, whereas eNOS levels decreased in the CIH arteries. CONCLUSION:: The current results suggest that endothelial dysfunction in CIH-induced hypertension may result from imbalanced arginase-1 to eNOS expression, vascular remodelling and increased contractile capacity, rather than decreased vascular response to nitric oxide.

arginase

chronic intermittent hypoxia

endothelial dysfunction

nitric oxide

vascular reactivity

acetylcholine

arginase 1

endothelial nitric oxide synthase

enzyme inhibitor

guanylate cyclase inhibitor

n(g) nitroarginine

nitric oxide donor

nitroprusside sodium

oxygen

potassium chloride

acetylcholine

arginase

arginase I, human

endothelial nitric oxide synthase

nitric oxide

nitric oxide donor

nitroprusside sodium

adult

animal experiment

animal model

animal tissue

artery endothelium

Article

blood pressure

blood vessel tone

chronic intermittent hypoxia

controlled study

endothelial dysfunction

enzyme inhibition

external carotid artery

hypertension

immunohistochemistry

internal carotid artery

isolation procedure

male

morphology

myography

nonhuman

priority journal

protein expression

rat

sensitivity analysis

vasodilatation

Western blotting

animal

anoxia

artery

drug effects

metabolism

pathophysiology

physiology

Sprague Dawley rat

vascular endothelium

Acetylcholine

Animals

Anoxia

Arginase

Arteries

Endothelium, Vascular

Male

Nitric Oxide

Nitric Oxide Donors

Nitric Oxide Synthase Type III

Nitroprusside

Rats

Rats, Sprague-Dawley

Vasodilation