Celastrol attenuates hypertension-induced inflammation and oxidative stress in vascular smooth muscle cells via induction of heme oxygenase-1.


Source
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Abstract

BACKGROUND:
The aim of this study was to investigate the potential beneficial effects of celastrol, a compound with anti-inflammatory and antioxidant properties, on vascular smooth muscle cells (VSMCs) under hypertensive conditions.

METHODS:
Hypertension was induced in rats by fructose feeding. Hypertensive rats were injected with celastrol, and systolic blood pressure (SBP) and diastolic BP (DBP) were monitored by the tail-cuff method. Insulin sensitivity in animals was measured by glucose tolerance test (GTT). Serum levels of inflammatory cytokines were determined by enzyme-linked immunosorbent assay. Real-time reverse transcription-PCR and western blot were applied to quantify mRNA and protein levels in tissues and primary cultured VSMCs. Generation of reactive oxygen species (ROS) was measured using lucigenin chemiluminescence for tissue homogenates and dichlorodihydrofluorescein diacetate staining for VSMC cells.

RESULTS:
Celastrol decreased both SBP and DBP while improving insulin sensitivity in fructose-induced hypertensive rats. Celastrol also inhibited vascular and cardiac hypertrophy. Hypertension augmented circulating and mRNA levels of inflammatory cytokines, and celastrol treatment suppressed their induction. Celastrol also blocked activation of extracellular signal-regulated kinase (ERK)/mitogen-activated protein kinase (MAPK) and Akt signaling both in vivo and in vitro. More importantly, celastrol increased heme oxygenase-1 (HO-1) expression and activity, whereas zinc protoporphyrin 9 (ZnPP9), a HO-1 inhibitor, partially abolished the beneficial effects of celastrol on hypertensive rats and VSMCs. Finally, ROS generation in tissue homogenates and in VSMCs was reduced by celastrol.

CONCLUSIONS:
These findings suggest that celastrol attenuates hypertension-induced inflammation and oxidative stress in VSMCs via HO-1 induction, and this compound may therefore serve as a novel drug to treat hypertension.
- **HO-1 attenuates hypertension-induced inflammation/oxidative stress: support from Bartter's/Gitelman's patients.** [Am J Hypertens. 2010]
- **Celastrol: a new therapeutic potential of traditional Chinese medicine.** [Am J Hypertens. 2010]

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