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Histone deacetylase inhibitor CG200745 ameliorates high fat diet-induced hypertension via inhibition of vascular smooth muscle contraction

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Objectives: Obesity is a major risk factor of hypertension. Histone deacetylases (HDACs) play a protective role in cardiovascular disease by regulating histone/non-histone protein deacetylation. The purpose of this study is to investigate the role and underlying mechanism of HDAC inhibitor CG200745 in high fat diet(HFD)-induced hypertension.

Methods: Nine-week-old male C57BL/6 mice were fed with 60% fat diet or normal diet (ND) for 17 weeks. When the HFD group reached hypertensive phase, CG200745 was administered for 8 days (200 $\mu g \cdot kg^{-1} \cdot day^{-1}$, i.p.). Body weights (BW) and blood pressure (BP), serum concentration of angiotensin II (Ang II), status of contractile proteins in aorta were determined.

Results: HFD group showed greater BW (45.1 ± 1.2 g) compared with ND group (34.0 ± 0.7 g)(p<0.001, ND vs HFD). HFD group showed higher systolic BP (144.3 ± 3.5 mmHg) compared with ND group (115.9 ± 1.8 mmHg)(p<0.001, ND vs HFD) and diastolic BP (111.5 ± 5.3 mmHg) compared with ND group (87.6 ± 1.1 mmHg)(p<0.001, ND vs HFD). HFD group showed higher serum Ang II concentration (15.2 ± 2.6 ng/mL) compared with ND group (1.7 ± 0.2 ng/mL)(p=0.001, ND vs HFD). HFD also increased phosphorylation of PKC-potentiated inhibitory protein of PP1 (CPI-17) resulting in phosphorylation of myosin light chain (MLC_{20}). CG200745 administration lowered blood pressure in HFD group. CG200745 also decreased serum Ang II level and phosphorylation of CPI-17 and MLC_{20}.

Conclusions: In conclusion, CG200745 ameliorates HFD-induced hypertension via decrease in Ang II and smooth muscle contraction. Our results offer CG200745 as a novel therapeutic option for HFD-induced hypertension.