Artery Research
Vol. **25**(**S1**); 2019, *p.* S46
DOI: https://doi.org/10.2991/artres.k.191224.039; ISSN 1872-9312; eISSN 1876-4401
https://www.atlantis-press.com/journals/artres

P4 Aldosterone-Induced Vascular Dysfunction by Decreasing Nuclear Factor Erythroid 2–Related Factor 2 Activity and Increasing Reactive Oxygen Species Generation

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ABSTRACT

Introduction: Chronic increases in aldosterone (Aldo) levels (hyperaldosteronism) increases blood pressure and induces hypertension. In the cardiovascular system, Aldo stimulates reactive oxygen species (ROS) generation. ROS contribute to vascular dysfunction by increasing vascular smooth muscle contractile tone, among other effects. Nuclear factor erythroid 2–related factor 2 (Nrf2), it's one of the main factors in the adaptive response to oxidative stress.

Hypothesis: Aldo negatively regulates the antioxidant system Nrf2, favoring ROS accumulation and subsequent vascular dysfunction.

Methods: Vascular function was evaluated in mice aortic conductance arteries, by performing concentration-effect curves to phenylephrine (PE) and acetylcholine (ACh). ROS production, determined by lucigenin and AmplexRed chemiluminescence, and Nrf2 activity by a nuclear translocation assay, were determined in endothelial cells (EA.hy926).

Results: Aldo increased PE contractions and decreased the relaxation response to ACh. L-sulforaphane, a Nrf2 activator, prevented Aldo-induced vascular dysfunction. In endothelial cells, Aldo increased ROS generation, i.e. superoxide anion and hydrogen peroxide, in a time-dependent manner. In addition, Aldo increased Nrf2 translocation at 30 min, 1 and 3 hours. However, after 3 hours, Aldo decreased Nrf2 translocation.

Conclusion: These data indicate that Aldo increases ROS in endothelial cells and causes impairment in vascular reactivity, events associated with decreased Nrf2 activity. Financial support: FAPESP (Process Number: 2018/05298-1), CAPES, CNPq. This study was approved by the Ethics Committee on Animal Experimentation of the Ribeirao Preto Medical School (030/2018).

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