EFFECT OF CADMIUM ON NITRIC OXIDE SYNTHESIS IN HUMAN CORONARY ARTERY ENDOTHELIAL CELLS

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ABSTRACT

Cadmium exposure is a risk factor for a variety of vascular disorders such as hypertension, ischemic heart disease and atherosclerosis. Cadmium-exposed subjects have increased oxidative stress and reduced nitric oxide (NO) bioavailability representing endothelial cell (EC) dysfunction. To further elucidate the mechanism, the potential plasma NO consumption and thrombomodulin (a marker of EC dysfunction) were determined in plasma of cadmium-exposed subjects. Additionally, the effect of cadmium on NO production in EC was studied in vitro using human coronary artery EC (HCAEC). Potential NO consumption by plasma of cadmium-exposed and control subjects was not different. Cadmium-exposed subjects had increased thrombomodulin levels compared to controls. 50% toxic concentrations of cadmium on HCAECs were in the range of 64-135 μM. Cadmium (0.1 μM) attenuated acetylcholine-stimulated NO synthesis in HCAEC and blocked endothelial NO synthase (eNOS) phosphorylation at serine1177 which was associated with increased eNOS activity. However, cadmium had no effect on eNOS mRNA and protein levels. In conclusion, cadmium-exposed subjects had EC dysfunction associated with reduced NO bioavailability. Inhibition of eNOS phosphorylation by cadmium may lead to diminish eNOS activity and NO synthesis.

KEY WORDS: CADMIUM/ ENDOTHELIAL CELL/ ENDOTHELIAL NITRIC OXIDE SYNTHAE

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