Inhibition of angiotensin II induced endothelin-1 gene expression by 17-beta-oestradiol in rat cardiac fibroblasts

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摘要

Abstract

OBJECTIVE: To examine whether 17-beta-oestradiol (E(2)) may alter angiotensin II (Ang II) induced cell proliferation and to identify the putative underlying signalling pathways in rat cardiac fibroblasts. DESIGN: Cultured rat cardiac fibroblasts were preincubated with E(2) then stimulated with Ang II. [(3)H]Thymidine incorporation and endothelin-1 (ET-1) gene expression were examined. The effect of E(2) on Ang II induced NADPH oxidase activity, reactive oxygen species (ROS) formation, and extracellular signal regulated kinase (ERK) phosphorylation were tested to elucidate the intracellular mechanism of E(2) in proliferation and ET-1 gene expression. RESULTS: Ang II increased DNA synthesis, which was inhibited with E(2) (1-100 nmol/l). E(2), but not 17-alpha-oestradiol, inhibited Ang II induced ET-1 gene expression as shown by northern blotting and promoter activity assay. This effect was prevented by co-incubation with the oestrogen receptor antagonist ICI 182,780 (1 micromol/l). E(2) also inhibited Ang II increased NADPH oxidase activity, ROS formation, ERK phosphorylation, and activator protein-1 mediated reporter activity. CONCLUSIONS: The results suggest that E(2) inhibits Ang II induced cell proliferation and ET-1 gene expression, partially by interfering with the ERK pathway through attenuation of ROS generation. Thus, this study provides important new insight regarding the molecular pathways that may contribute to the proposed beneficial effects of oestrogen on the cardiovascular system.