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

陳正憲

Chao HH;Chen JJ;Chen CH;Lin H;Cheng CF;Lian WS;Chen YL;Juan SH;Liu JC;Liou JY;Chan P

摘要

Abstract

Objective: To examine whether 17-ß-oestradiol (E2) 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 E2 then stimulated with Ang II. [3H]Thymidine incorporation and endothelin-1 (ET-1) gene expression were examined. The effect of E2 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 E2 in proliferation and ET-1 gene expression. Results: Ang II increased DNA synthesis, which was inhibited with E2 (1–100 nmol/l). E2, but not 17--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 µmol/l). E2 also inhibited Ang II increased NADPH oxidase activity, ROS formation, ERK phosphorylation, and activator protein-1 mediated reporter activity. Conclusions: The results suggest that E2 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.