P2 THE INDUCTION OF COX-2 IN 17β-ESTRADIOL TREATED ENDOTHELIAL CELLS IS MEDIATED BY PROTEIN KINASE C.

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ABSTRACT

Cyclooxygenase (COX), which exist as COX-1 and COX-2 isoform, is the first enzyme in the pathway in which arachidonic acid is converted to prostaglandins including PGI_2. Previously, we showed that 17β-estradiol stimulates the production of prostacyclin (PGI_2), a potent vasodilator and platelet inhibitor, through the induction of COX-2 in endothelial cells. However, the signalling mechanism of COX-2 induced in 17β-estradiol activated endothelial cells has not been clearly identified. Here, we have used protein kinase inhibitor (staurosporine) as pharmacological tool to investigated the signalling mechanism of COX-2 induced in human umbilical vein endothelial cells (HUVEC) treated with 17β-estradiol. COX activity was measured by the production of 6-keto-$PGF_{1\alpha}$ (stable metabolites of PGI_2) using enzyme immunoassay. COX-2 protein expression was detected by using immunoblotting. 17β-estradiol (0.001, 0.01, 0.1 and 1 nM) increased COX activity by the production of 6-keto-$PGF_{1\alpha}$ in a dose dependent manner. Interestingly, COX-2, but not COX-1, was induced in 17β-estradiol treated HUVEC. This induction was increased in a dose dependent manner. Moreover, the induction of COX-2 in 17β-estradiol treated HUVEC was inhibited when cells were coincubated with staurosporine (protein kinase C inhibitor; 0.01, 0.1 and 1 μM). This inhibition was inhibited in a dose dependent manner. The increased COX activity in HUVEC treated with 17β-estradiol was also inhibited by staurosporine (0.01, 0.1 and 1 μM) in a dose dependent manner. These results suggested that the increased COX activity in 17β-estradiol treated HUVEC was mediated COX-2 induction via protein kinase C.