บทคัดย่อ (Abstract)

Estrogen stimulates the production of prostacyclin (PGI_2), a potent vasodilator and platelet inhibitor which plays an important role in cardiovascular disorder. PGI_2 is produced under a regulatory enzyme called cyclooxygenase (COX), which exists as COX-1 and COX-2. The exact mechanism of rising PGI_2 in endothelium by estrogen has not been clearly identified. Here, we have investigated whether estrogen affects COX isoform expressed in human umbilical vein endothelial cells (HUVEC). HUVEC were grown to confluent and replaced with fresh medium containing 17β-estradiol (0.01, 0.1 and 1 nM) or 17β-estradiol (1 nM) plus staurosporin (0.1, 1 and 10 ng/ml) for 24 h. After which time, the supernatant medium was collected to measured 6-keto-$PGF_{1\alpha}$ using enzyme immunoassay. To measured COX activity via exogenous substrates, The remained cells were replaced with fresh medium containing arachidonic acid (10 μM for 10 min) and, then, the medium was removed to measured 6-keto-$PGF_{1\alpha}$. The COX isoform expressed in cells was detected by immunoblotting using specific antibody. 17β-estradiol (0.001 to 1 nM) increased the production of 6-keto-$PGF_{1\alpha}$ either via endogenous or exogenous substrate in a dose dependent manner. These increase was inhibited significantly when cells were coincubated with staurosporin. Interestingly, COX-2 protein, but not COX-1 protein, was induced in 17β-estradiol treated HUVEC which was also inhibited by staurosporin. Thus, 17β-estradiol increased the release of PGI_2 from HUVEC via the induction of COX-2 which was mediated through protein kinase C. The results suggested that COX-2 may have role in the cardiovascular protective effects of estrogen.