I S—57 EFFECT OF ENDOTHELIN ON THE PAF ACETYLHYDROLASE SECRETION BY HUMAN DECIDUAL MACROPHAGES.

Oita Medical University
Hisashi Narahara, Kenichiro Urata, Kazuyo Arima, Yuichiro Tanaka, Isao Miyakawa

[Objective] To clarify the role of platelet-activating factor(PAF) in parturition, we have investigated the effect of endothelin (ET) on the PAF metabolism in the decidua.
[Methods] The decidual macrophage (Mφ) populations were obtained from term human decidua by enzymic digestion, Ficoll-Paque centrifugation, or flow cytometric sorting. The effects of ET-1, ET-2, ET-3, and/or their neutralizing antibodies on the secretion of a PAF-inactivating enzyme, PAF-acetylhydrolase(PAF-AH), by these cells were examined. The enzyme activity was assayed by the method of Miwa et al..
[Results] ET-1 inhibited PAF-AH secretion by either decidual cells(IC50=1.5±0.2 nM, n=6) or flow cytometrically purified decidual Mφ ET-2 and ET-3 also inhibited the enzyme secretion, however, the effect was seen only at ten times higher concentrations than required for ET-1-induced inhibition. The ET-1-induced inhibition was abolished by an anti-ET-1 antibody. Protein kinase C(PKC) inhibitors, sphingosine and H-7 partially blocked the inhibition by ET-1.
[Conclusions] It is suggested that ET may increase the biological activity of PAF in the decidua via its inhibitory effect on the PAF-AH secretion by decidual Mφ and that the inhibitory effect may, in part, be mediated by PKC dependent signal transduction.

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Attenuation of vasoconstriction by estrogen through endothelium-independent mechanism in human uterine artery

M. Hur, H.M. Park, S.Y. Park, Y.I. Lee, B.J. Jung

Dept. of Obstetrics and Gynecology,
School of Medicine, Chung-Ang University,
Seoul, Korea

Estrogen exerts a favorable influence on cardiovascular system through endothelium-dependent and independent mechanisms. The former may be mainly linked to the modulation of the release of vasorelaxants and/or vasoconstrictors from vascular endothelium, while little is known about the latter mechanisms.

Objective : This study was performed to investigate whether 1) estrogen induces the change of vascular tone in endothelium-denuded human uterine artery, and 2) endothelium-independent vascular reactivity may be mediated by intracellular calcium ion modulation.

Methods : The uterine arteries from 34 premenopausal women were obtained at the time of hysterectomy due to various indications and endothelium was denuded. Vascular reactivity was monitored by using Isometric force transducer and recorded by physiograph. Endothelial integrity was assessed by sequential administration of 1μM norepinephrine(α-adrenergic stimulant) and 10μM acetylcholine(endotelium-dependent vasorelaxant). Integrity of smooth muscle was measured by administration of 10μM sodium nitroprusside(endotelium-independent vasorelaxant) and 10 μM tamsulosin(α-adrenergic blocker). A dose-dependent action of estrogen was measured on denuded uterine arteries, pretreated with norepinephrine and potassium chloride. In media contained denuded uterine arteries pretreated with 70mM potassium chloride and estrogen(3×10-5M), nitric oxide and its inhibitor, L-NAME was administered respectively, in order to verify the vasodilation effect.

Results : Acethylcholine have little effect but sodium nitroprusside & talmsulosin showed marked relaxation, which suggested loss of endothelial function and adequacy of smooth muscle function. The contraction by norephinephrine(1μM) revealed estrogen induced relaxation which was concentration-dependent from 3×10-8M to 3×10-5M in concentration of 17β-estradiol. The contraction by high potassium solution 70mM was also inhibited by estrogen in concentration-dependent manner. This vasorelaxant effect of estrogen on endothelium-denuded uterine artery was not affected by addition of NO precursor, L-arginie and NOS inhibitor, L-NAME.

Conclusion : the results of this study revealed that estrogen has vasorelaxant effect on endothelium deneded uterine artery by calcium antagonistic property through direct inhibitory effect on receptor- and voltage dependent calcium ion channels of smooth muscles. This vasorelaxant effect of estrogen on endothelium-denuded uterine artery was NO independent.