17beta-estradiol 抑制血小板凝集作用之機轉探討

Mechanisms involved in the antiplatelet activity of 17beta-estradiol

中文摘要

近幾年來的研究發現停經後婦女長期使用賀爾蒙療法會增加靜脈血栓以及增加心肌梗塞和缺血性中風這些疾病的危險性。然而賀爾蒙補充療法和加成性的賀爾蒙補充療法已經廣泛的被用來預防心血管疾病和血栓產生。這和目前的發現是互相矛盾的，所以我們對於 17beta-estradiol 如何調節血小板的活性感到興趣。

經由一系列實驗後，我們發現 17beta-estradiol (50-80 micro M)明顯的抑制 collagen 所引起的人類血小板凝集反應，但對於 thrombin 和 U46619 所引起的血小板凝集並沒有抑制的效果；17beta-estradiol (50-80 micro M)可以抑制由 collagen 所刺激細胞內鈣離子的流動和 thromboxane A2 的形成；17beta-estradiol (50-80 micro M)能抑制由 collagen 所引起的 PLC2 的磷酸化，進而去影響 47 kD 磷酸化，但對於由 PDBu 所引起 47 kD 磷酸化卻沒有影響，同時它也能增加 NO 的形成以及 VASP 的磷酸化，進而抑制血小板的凝集；再者 17beta-estradiol (50-80 micro M)並不會對 collagen 所引起的 p38 MAPK、ERK1/2 的磷酸化造成影響。在我們的實驗中發現，17beta-estradiol 抑制 collagen 所引起的的血小板活化，這個血小板凝集的機轉，主要是透過抑制 PLC2 的活性，進而抑制 PKC 的磷酸化，接著抑制 TxA2 的形成，最後導致細胞內減少鈣離子，所以抑制血小板的凝集；另一方面 17beta-estradiol 會增加 NO 的產生，使 cGMP 產生，且 17beta-estradiol 也會使 cAMP 產生，進而抑制血小板的凝集，其他更詳細的機轉將會更清楚的說明。

英文摘要

Post-menopausal hormone therapy increases the risk of venous thrombosis, and possibly myocardial infarction and ischemic stroke. However, estrogen replacement therapy or combined hormone replacement therapy has been widely used to protect against development of both cardiovascular diseases and other thrombotic diseases. Therefore, we are interested to evaluate whether 17beat-estradiol can regulate platelet activities. In this study, we found that 17beta-estradiol (50-80 micro M) significantly inhibited collagen (1 micro g/ml) but not thrombin (0.02 U/ml) or U46619 (0.1 micro M)-induced platelet aggregation in washed human platelets; 17beta-estradiol (50-80 micro M) markedly inhibited collagen (1 micro g /ml)-triggered calcium mobilization and thromboxane A2 (TxA2) formation in washed human platelets; 17beta-estradiol (50-80 micro M) significantly inhibited collagen- but not PDBu-induced 47-kDa protein phosphorylation; 17beta-estradiol also inhibited collagen-induced PLC2 phosphorylation; in addition 17beta-estradiol (50-80 micro M) also increased NO formation and induced phosphorylation of vasodilator-stimulated phosphoprotein(VASP). In conclusion, we showed that estradiol inhibited collagen-induced platelet aggregation. The anti-aggregatory

mechanism of 17beta-estradiol occurs via reducing PLC2 phosphorylation, TxA2 formation, calcium mobilization and increasing NO, cGMP and cAMP in washed human platelets. However, the more detailed anti-aggregatory mechanism of 17beta-estradiol will be elucidated in the future.