Abstract

Amira M. Senbel

In search of pulmonary hypertension treatments: Effect of 17?-estradiol on PGI2 pathway in human pulmonary artery.

Introduction: Prostacyclin (PGI2) is synthetized by PGI2 synthase (PGIS) and induces vasorelaxation via activation of cyclic AMP (cAMP) generating IP-receptor. Several components of the PGI2 signaling pathway are reduced in patients with pulmonary hypertension (PH). Aim: To study the effect of 17?-estradiol (E2) on the PGI2 signaling pathway in human pulmonary arteries (HPA) and in their smooth muscle cells (hPASMC) derived from Group-3 PH and non-PH patients. Methods: Following E2-treatments of isolated HPA and cultured hPASMC, we measured: 6-keto-Prostaglandin F1? (PGI2 stable metabolite) by ELISA, PGIS and IP protein levels by Western blot and HPA vasorelaxations with an organ bath system. Results: Incubation with E2 (24/48 h, doses ? 10 nM) significantly increased the expression of PGIS in hPASMC derived from both PH (65-98%) and non-PH (21-33%) patients, whereas incubation with E2 (2 h, 0.1 and 1 µM) increased 6-keto-PGF1? production in HPA from Group-3 PH patients only, and did not affect 6-keto-PGF1? production in hPASMC from either non-PH Group-3 PH patients. Increases in IP receptor expression were observed following 10 mM E2-treatment of hPASMC from non-PH (33% after 48 h) and Group-3 PH (23% after 24 h) patient lungs. Finally, preincubation with 100 nM E2 significantly increased arachidonic acid-induced vasorelaxation of HPA from non-PH patient lungs but not of HPA from Group-3 PH patient lungs. Conclusion: E2-treatment may help to restore the PGI2-pathway in Group-3 PH. Keywords: 17?-estradiol Human pulmonary artery Human pulmonary artery smooth