EP3 receptor is involved in the PGE2-induced contraction of human intercostal arteries

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Prostanoids are involved in the control of human vascular tone. Prostaglandin E2 receptors (EP1 or EP3) are associated with vasoconstriction and they have been described in human pulmonary vessels and in mammary artery (Norel, 2007). The aim of this study was to determine which PGE2 receptors are responsible for the contraction of human intercostal arteries (HIA).

HIA dissected from aorta (obtained from anonymous dead donors, with the authorization of the French Biomedicine Agency, Bichat and Saint-Louis Hospitals, Paris, France) were cut into rings and set up in organ baths with Tyrode's solution and equilibrated for 90 min. Changes in force were recorded using isometric transducers and physiographs. Cumulative dose response curves (1 nM – 0.1 mM) were obtained with one of the following agonists (EP1/3): PGE2, sulprostone, 17-phenyl-PGE2, misoprostol, ONO-AE-248 or ONO-DI-004. These curves were produced in presence of indomethacin (17 µM), L-NOARG (0.1 mM), a TP-antagonist (BAY u3405, 10 µM) and with or without one selective antagonist (ONO-8713, EP1; L-826266, EP3). Results are means\textpm{s.e.m.} derived from n individuals and paired Student's t test was used for the statistical analysis.

The data show that PGE2 induced contractions (Emax = 0.80\textpm{}0.18 g; pEC50 = 7.29\textpm{}0.22; n=11) represent about 75\% of those induced by norepinephrine 10 µM. The PGE2 induced contractions were inhibited by L-826266 but not by ONO-8713. The involvement of the EP\textsuperscript{3} receptor in HIA contraction was supported by the following observations. First, ONO-AE-248 and misoprostol, selective EP\textsuperscript{3} agonists always induced contractions in HIA. Second, the potency ranking for previously documented agonists was sulprostone (pEC50 = 7.90\textpm{}0.22; n=6) > 17-phenyl-PGE2 (pEC50 = 6.75\textpm{}0.19; n=6). These results support the notion of EP\textsuperscript{3} receptor rather than EP\textsuperscript{1} receptor activation for this vasoconstriction

In conclusion, these results are in accordance with the activation of EP3- and not EP1- receptors during the PGE2-induced contraction of human intercostal arteries. PGE2 could play a role in spinal cord vulnerability to changes in blood and cerebrospinal fluid pressure.

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