Role of secretory phospholipase A₂ in rhythmic contraction of pulmonary artery of experimental pulmonary hypertension

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Excessive stretching of the vascular wall in accordance with pulmonary arterial hypertension (PAH) induces a variety of pathogenic cellular events in the pulmonary arteries. The present study was undertaken to investigate involvement of secretory phospholipase A₂ (sPLA₂) and untransformed prostaglandin H₂ (PGH₂) in the enhanced contractility of pulmonary arteries of experimental PAH in rats.

Among all the known isoforms of sPLA₂, sPLA₂-X transcript is significantly augmented in the pulmonary arteries of rats with monocrotaline-induced pulmonary hypertension (MCT-PHR). The pulmonary arteries of MCT-PHR frequently showed two types of spontaneous contraction in response to stretch; 27% showed rhythmic contraction, which was sensitive to indoxam (selective sPLA₂ inhibitor) and SC-560 (selective cyclooxygenase-1 inhibitor), but insensitive to NS-398 (selective cyclooxygenase-2 inhibitor); and 47% showed sustained incremental tension (tonic contraction), which was insensitive to indoxam and SC-560 but sensitive to NS-398 and was attenuated to 45% of control. Only the rhythmically contracting pulmonary arteries of MCT-PHR produced a substantial amount of untransformed PGH₂, which was abolished by indoxam. In addition, cyclic stretching of cultured rat vascular smooth muscle cells significantly induced several sPLA₂ transcripts, including sPLA₂-X.

These results suggested that the mechanically-induced sPLA₂ plays an important role in the PGH₂-dependent rhythmic contraction of pulmonary arteries of MCT-PHR.