Enzymes responsible for PGE2 synthesis in human saphenous varicose veins

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Varicose saphenous veins are elongated and dilated veins. They are characterized by venous backflow, blood stagnation and vascular wall remodelling but the inflammatory condition remains unclear. In western countries, this pathology affects approximately one-third of the adult population, however, the pathogenesis of varicosity formation is unclear. PGE2 is obtained from arachidonic acid metabolism by cyclooxygenases (COX-1, COX-2) and by PGE synthase (PGES) isoenzyme: microsomal PGES (mPGES) -1, -2 and cytosolic PGES (cPGES). Several studies showed that PGE2 production is upregulated in inflammatory conditions, in these cases mPGES1 is mainly responsible for PGE2 synthesis by interaction with COX-2. Other studies have shown that PGE2 is involved in vascular wall remodelling (via MMP activities, Cipollone et al., 2001) and is able to induce vasodilatation. That could be one cause of varicose vein formation.

AIM: The aim of the present work was to study the enzymes responsible for Prostaglandin E2 (PGE2) synthesis in varicose veins.

METHODS: In order to study the expression of different COXs and PGESs, proteins and mRNA were extracted from human saphenous veins (large and small diameter varicosities from the same patients or healthy donors) obtained at Bichat hospital (Paris). Expressions of these enzymes were compared by Western blot analysis and Real Time PCR. Using histomorphometry we have measured the collagen content on formalin-fixed venous preparations.

RESULTS: COX-1/-2, mPGES -1 and -2 are expressed in varicose and healthy saphenous veins. However, we observed a significant decreased expression, approximately 50%, of mPGES1 in varicose veins (large diameter varicosity) with regard to the healthy and less pathological preparations (small diameter varicosity). We also observed that mPGES1 mRNA correlated positively with COX-1 mRNA ($R^2=0.869$) but not with COX-2 ($R^2=0.0085$). In addition, we observed a significant increase (almost 50%) in collagen content in large diameter varicosities.

CONCLUSION: PGE2, involved in vascular wall remodelling via MMP activities, participates in matrix degradation. In contrast to our expectations, mPGES1 content is decreased in large diameter varicosities compared to small ones and healthy saphenous veins. The mPGES1 decrease should be associated with a reduced MMP activity and would explain the increased collagen quantity observed. These results show that PGE2 and PGES play a role in varicosity formation. Furthermore, in contrast to previously published results, mPGES1 seems to be co-expressed with COX-1 and not COX-2 in this tissue.