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i2 SUMMIT

UPREGULATION OF HYPOXIA-INDUCIBLE FACTOR BY DI-METHYL OXALYL GLYCINE (DMOG) INCREASES NEOVASCULARIZATION WITHIN ISCHAEMIC MYOCARDIUM IN A PORCINE CORONARY OCCLUSION MODEL

i2 Poster Contributions
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Background: Chronic total coronary artery occlusion (CTO) remains a significant challenge for percutaneous coronary intervention (PCI), and a common reason for referral for coronary bypass surgery. This study was designed to investigate a potential alternative treatment strategy for CTO through promotion of antegrade collaterals around the CTO. We investigated the effect of the prolyl-4-hydroxylase inhibitor di-methyl oxalyl glycine (DMOG) and thus a HIF 1α promoter on collateral vessel formation in a novel endovascular porcine model of coronary occlusion.

Method: DMOG was loaded onto a polymer-coated coronary stent. A percutanous model employing copper-coated stents was used to produce CTO lesions in 20 Yorkshire white pigs. DMOG stents were implanted at day 28 and angiographic and physiological data collected on distal coronary and collateral flow. At day 56 the animals were sacrificed and histological analysis performed.

Results: A complete total coronary occlusion was present in all animals at day 28 following implantation of a copper stent. At 56 days there was a larger increase in angiographic collateral area in the DMOG group vs. controls (10±4.1 mm2 increase vs. 3.6±1.5mm2; 84.5% vs. 16.5% increase, p=0.057). Collateral flow index increased in the study group as a whole from day 0 to day 28 post-copper stent (0.12±0.02 to 0.4±0.04, p<0.001) but there was similar distal perfusion in both groups at day 56. Histology revealed an increase in collateral number (vessels >100µm diameter) seen around the site of occlusion in the DMOG group (29.9±2.6 vs. 18.4±3.1, p=0.01).

Conclusion: DMOG increases the number of collateral vessels seen at the site of vessel occlusion but did not increase neovascularization in distal tissue. At baseline distal myocardium was subtended by extensive antegrade collaterals. The effect of DMOG in increasing neovascularization appeared to be resticted to ischaemic tissue. Implantation of a copper stent provides a reliable entirely endovascular method of producing a CTO with marked antegrade collateral formation at 28 days. Proximal placement of stents delivering angiogenic compounds may provide a clinical management option in resistant CTO lesions.