Prolonged Clopidogrel Treatment Reduces Lesion Cell Proliferation After Balloon Injury and Intracoronary Radiation

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BACKGROUND: Prolonged Clopidogrel therapy after intracoronary radiation (IR) treatment in stent restenosis has been shown to reduce major adverse clinical events (MACE). This beneficial effect has been mainly contributed to the antithrombotic mechanism, but it is unknown whether the P2Y12 receptor antagonist mediates additional effects preventing MACE. The purpose of our study was to analyze the effect of prolonged Clopidogrel treatment on cell proliferation in the intimal/medial vascular lesion (I+M VL) of balloon-injured coronary arteries with or without beta-IR. METHODS: 24 porcine coronary arteries were subjected to balloon injury (PTCA) of which 12 arteries underwent immediate irradiation using a source train of 90S/Y seeds delivering 20 Gy at a depth of 2 mm from the source. Animals were divided into two groups, one group receiving 4 weeks Clopidogrel treatment (28dCl) and the second 3 months (90dCl). Bromo-deoxyuridine (BrdU) was administered one hour prior to euthanasia to label proliferating cells. Coronary artery lesions were immunohistochemically examined 3 months after injury. RESULTS: Cell proliferation in the I+M VL of balloon-injured coronary arteries with or without beta-IR was significantly lower in the 90dCl group (PTCA+IR:18.40 ± 2.17 proliferating cells/mm² in the 90dCl group vs. PTCA: 16.2 ± 6.55 proliferating cells/mm² in the 28dCl group, p<0.05). Total plaque percent (=vessel-lumen volume/vessel volume%) at non-stented sites, at baseline and follow-up, was: S: 49.8±3% and 39.9±7%, and P: 51.1±2 and 57.1±11% (p<0.05). External plaque volume index (=vessel-stent volume/stent length), at baseline and follow-up, was: S: 11.9±4.2 and 7.9±3.3 mm³/mm, and P: 10.9±4.0 and 11.6±3.5 mm³/mm (p<0.05). Total plaque percent (=vessel-lumen volume/vessel volume%) at stented sites, at baseline and follow-up, was: S: 53±10 and 39.9±7%, and P: 51.1±2 and 57.1±11% (p<0.05). External plaque volume index (=vessel-stent volume/stent length), at baseline and follow-up, was: S: 9.8±3.6 and 7.3±2.5 mm³/mm, and P: 8.8±2.9 and 9.8±3.1 mm³/mm (p<0.05). CONCLUSION: In normocholesterolemic patients, prolonged treatment with oral simvas- tatin shows no effect in preventing IR and neointimal growth after coronary stenting. However, it reduces MACE and induces a diffuse regression of the atherosclerotic plaque burden.

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