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A Lesson of Vascular Biocompatibility: Titrating biodegradable polymer coating and drug

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Background: Our previous work demonstrated a sequence of medial necrosis, stent malapposition, and late neointimal thickening, with a moderate paclitaxel dose eluted from an erodible polymer. The use of slower releasing absorbable polymers with lower doses of paclitaxel, and modifying polymer/drug ratio are expected to minimize such adverse outcomes.
Aim: To evaluate a new second-generation DES, comprising a slow release biodegradable PLGA polymer and low dose paclitaxel on a thin strut cobalt chromium stent platform.
Methods: Three types of stents were implanted in pig coronaries: BMS; absorbable, slow release polymer coated-only stents (POLY); and absorbable polymer-based paclitaxel eluting stents (PACL). The dose density of paclitaxel was 0.15μg/mm² with in vitro studies demonstrating a gradual elution over 12-16 weeks. Animals underwent angiographic restudy and were terminated at 1 and 3 months for histological analysis.
Results: At 1 month, angiographic % stenosis was significantly lower for PACL compared with BMS and POLY groups (2±2% vs. 12±4% and 11±10%, respectively, p<0.001); intimal thickness varied significantly according to stent type, with the lowest level for the PACL group compared with the BMS and POLY groups (0.06mm±0.02 vs. 0.17mm±0.07, 0.17mm±0.08, respectively, P<0.001); histological % area stenosis was 18%±4 for PACL compared with 27±7% for BMS and 30±12% for POLY, respectively (p=0.001). At 3 months, PACL showed similar neointimal thickness as BMS and POLY (0.09mm±0.05 vs. 0.13mm±0.10 and 0.11mm±0.03 respectively, P=0.582).

Conclusions: Favorable vascular compatibility and efficacy for a new DES that elutes paclitaxel from a slow release bioabsorbable polymeric surface coating were demonstrated. Our results furthermore suggest that the rate of release rather than the total drug load on the stent is the major factor which determines whether the mode of neointimal suppression is toxic or non-toxic in nature.