TCT-444

Anti-inflammatory Effect of Arsenic Trioxide Eluting Stents in a porcine coronary model

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Background: Previous research from our group has demonstrated trioxide (As2O3) eluting stents significantly reduce neointimal area and thickness compared with bare metal stents. In the present study, we explored the anti-inflammatory effect of As2O3 in vitro and in vivo for understanding the mechanism of AESs in reducing in-stent restenosis.

Methods: Human dendritic cells and T lymphocytes were co-cultured with different concentrations of As2O3. Effect of As2O3 on apoptosis, phenotype characterization, and cytokines production of these two kinds of inflammatory cells were evaluated by flow cytometry and enzyme-linked immunosorbent assays. Fifty-five pigs underwent placement of 139 oversized stents in the coronary arteries with histologic analysis, As2O3 levels evaluation, endothelial function analysis, immunohistochemical and western blot analysis.

Results: As2O3 induced apoptosis of human T lymphocytes and dendritic cells in a dose-dependent manner. AESs reduced less foreign body reactions of fibrin-platelet deposition and acute inflammatory cells infiltration than BMSs and polymer-coated stents (PCSs). There was no significant difference in extensive endothelialization between AESs and BMSs after 4 weeks post stent implantation. Stent-based As2O3 delivery effectively inhibited expression of inflammation-associated proteins such as monocyte chemoattractant protein-1 (MCP-1) and interleukin-6 (IL-6), in agreement with the western blotting results.

Conclusion: Stent-based As2O3 delivery effectively inhibited expression of inflammation in vitro and in vivo for understanding the mechanism of AESs in reducing in-stent restenosis.

TCT-445

Optical Characteristics of Neointimal Formation Correlate with Histological Markers of Stent Healing in a Porcine Model of Restenosis

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Background: Optical coherence tomography (OCT) has the ability to detect small changes in peri-stent neointimal formation, however, its ability to characterize tissue types is still limited. In this study, we aimed to compare different characteristics of in-stent neointimal tissue using OCT types analysis and histology.

Methods: A total of 69 stents [39 DES and 30 BMS] were implanted in coronary arteries of 27 swine. By OCT, neointimal type was classified as homogenous, heterogeneous or layered pattern according to its pattern of backscatter and optical density. Appearances of Reader resulting optical patterns were correlated with histological findings (external elastic lamina (EEL) disruption, significant fibron deposition, circumferential rim of peri-stent inflammatory cell infiltration and collagen deposition) in every cross section (CS).

Results: A total of 197 OCT and histological CS were well matched. The heterogeneous pattern (0.44±0.21 mm) and layered (0.65±0.16 mm) patterns had a significantly higher degree of neointimal thickness compared to the homogenous pattern (0.25±0.16 mm, p<0.001). Collagen deposition was more frequently present in the homogenous pattern (72%), whereas significant fibron deposits were more commonly seen in the heterogeneous pattern (57%). Peri-stent inflammation was less frequently found in the homogenous pattern (19.8%) in comparison to the layered (73.9%) or heterogeneous patterns (43.1%). Presence of EEL rupture behaved similarly (73.9% in layered, 46.6% in homogenous, 22.4% in heterogeneous pattern). Optical density and area was found to be the homogenous pattern had the narrowest standard deviation (0.99±0.10 vs 0.26±0.22 in heterogeneous and 0.42±0.24 in layered pattern) and the highest mean value (105.9±17.6 vs. 83.0±17.1 in heterogeneous and 84.0±12.9 in layered pattern).

Conclusion: The optical characteristics of neointimal formation seen in OCT properly correlated with the presence of several histological findings involved in stent healing. The biological implications of these findings in clinical outcomes require further investigation.

TCT-446

Short-term effects of sirolimus eluting fully bioabsorbable polymeric coronary stents in a porcine model

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Background: Conventional metallic, drug-eluting stents (DES) restrict restenosis after percutaneous coronary intervention (PCI). However, stents can generate additional foreign body reactions and consequently increase the possibility of adverse events. Biodegradable scaffolds have been suggested as a possible solution. In the present study, short-term effects of fully bioabsorbable sirolimus-loaded poly-D-lactic acid (PLLA) stents (Xinsorb) were evaluated in a porcine coronary model to assess the technical feasibility, biocompatibility, and effects on coronary stenosis.

Methods: PLLA stents (Xinsorb, Huan Biotechnology Co., Ltd, China) were coated with 140 μg of sirolimus. Commercially available sirolimus-eluting stents (Excel, JW Medical System, China) were used as controls. Xinsorb stents (n=16) and Excel stents (n=16) were randomly implanted in porcine coronary arteries. Neointima formation was measured by angiography and histomorphometry at 30 and 90 days. Additional in-stent inflammation and endothelialization were measured.

Results: Xinsorb stents can be delivered and expanded at high pressure compared with Excel stents, without any fracture and acute recoil. Both had a remarkable effect on reducing neointimal hyperplasia, since no distinctive vessel narrowing greater than 50% were observed by angiography. Histomorphometry, at 30 and 90 days, coronary stenosis was 18.9±5.2 vs. 21.4±7.2% and 24.5±4.7% vs. 27.7±5.6% (p>0.05), after Xinsorb and Excel stent implantations. The inflammation scores were 0.84±0.15 vs. 0.74±0.10 and 0.93±0.26 vs. 0.88±0.10, respectively (p<0.05). At 90 days, through scanning electron microscopy, Xinsorb and Excel stents were all completely endothelialized, though they mildly delayed reendothelialization at 30 days. Conclusion: Xinsorb stents reliably supported blood vessels and favourably modulated neointimal formation at least at 90 days in a porcine coronary model. No safety concerns regarding inflammatory reactions and in-stent thrombosis were observed. The long-term safety and efficacy of the stents will be validated.

TCT-447

Angiographic and Histological Response Following Implantation of a Novel Stent-On-A-Wire in the Animal Model

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Background: The Svelte Stent-on-a-Wire (SOAW) is a thin strut novel device consisting of a balloon expandable cobalt chromium stent premounted onto a single lumen fixed-wire delivery catheter platform. We evaluated the performance of the novel Svelte Stent-on-a-Wire, in comparison with the MultiLink Vision (ML Vision) balloon expandable stent, in porcine coronary arteries.

Methods: Eight Yorkshire swine (30-day follow-up cohort) and 7 Yucatan mini-swine (90-day follow-up cohort) were implanted with either Svelte SOAW or control ML Vision. Acute performance characteristics were graded by interventionists during implantation. Angiographic assessments were performed at the index procedure and at 30 or 90 days post-implantation. Scanning electron microscopy (SEM) histological and histomorphometric analysis of stented segments were performed after angiographic follow-up.

Results: Acute implantation performance was similar between the 2 stents treatments at both time points. There was no in-stent thrombosis in either stent group. Histopathological assessment demonstrated minimal injury and equivalent inflammation at 30 and 90 days with Svelte SOAW and ML Vision stents as well as endothelialization, neointimal maturation, adventitial fibrosis and neointimal fibrin. Histomorphometric analysis showed no differences between the 2 groups in stent, lumen, media or neointimal areas at either 30 or 90 days post-implantation.

Conclusion: At 30 and 90 days after implantation in porcine coronary arteries, the