Intimal Hyperplasia Thickness Is Independent of Stent Size in Paclitaxel-Coated Stents: A Serial Intravascular Ultrasound Analysis From the Asian Paclitaxel-Eluting Stent Clinical Trial


Background: Intravascular ultrasound (IVUS) studies have shown that IH thickness is independent of bare metal stent size. This study determined whether intimal hyperplasia (IH) thickness within nonpolymeric paclitaxel-coated stents is dependent on stent size.

Methods: IVUS was performed post-stent implantation and at 6-months follow-up in 81 patients, 55 of which were randomized to the nonpolymeric paclitaxel-coated stent: 27 to bare metal stents.

Results: Overall, maximum IH CSA measured 2.15±1.58mm², mean IH CSA measured 0.93±0.31mm², maximum IH thickness measured 0.45±0.33mm, and mean IH thickness measured 0.33±0.21mm. There was a weak correlation between IH CSA vs stent CSA (r=0.196, p<0.0001), but no correlation between IH thickness vs stent CSA (r=0.052, p=0.138) on a per slice basis or between maximum IH CSA vs stent CSA (r=0.259, p=0.056) or maximum IH thickness vs stent CSA (r=0.07, p=0.6) on a per stent basis. The results were similar when high and low dose patients were analyzed separately on a per slice basis: (1) IH CSA vs Stent CSA (r=0.252, p<0.0001, and r=0.153, p=0.0013) and (2) IH thickness vs Stent CSA (r=0.126, p=0.015, and r=0.002, p=0.96).

Conclusions: IH thickness is independent of stent size in drug-eluting stents, similar to bare metal stents.

POSTER SESSION

1102
Restenosis: Basic Research I

Monday, March 08, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1102-47
Important Species Differences of Sirolimus, Paclitaxel, and Tacrolimus on Porcine and Human Coronary Smooth Muscle and Endothelial Cells

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Background: Implantation of drug coated stents shows clinical efficacy for the prevention of restenosis, but large animal studies have not shown any long term benefit with the use of Sirolimus (SiR) and Paclitaxel (PAC). Despite this the possible interspecies differences have not been investigated. Methods: Porcine (p) and human (h) smooth muscle (SMC) and endothelial cells (EC) were serum deprived for 48h until addition of drugs. Cells were counted after 72h of exposure to SiR, PAC or Tacrolimus (TAC) by means of a CASY cell counter on the basis of the resistance measurement principle. Cell viability was determined by means of MTT.

Results: Human SMC derived growth factor. 3) The area of neointima in the vehicle-treated group (n=23) was 0.132±0.010 mm² (mean±SEM), while that in the group treated with E5555 at 10 mg/kg (n=24) and 30 mg/kg (n=24) were 0.116±0.007 mm² (ns vs. vehicle) and 0.078±0.009 mm² (p<0.001), respectively. The ratio of neointimal to medial area was significantly decreased in the group treated with E5555 at 50 mg/kg (0.866±0.092 vs. 1.404±0.091 in vehicle, p<0.001) without affecting the medial area.

Conclusion: E5555, a potent and orally active PAR-1 antagonist, may be beneficial for the treatment of restenosis after percutaneous coronary intervention.

1102-48
Inhibitory Effect of E5555, an Orally Active Thrombin Receptor Antagonist, on Intimal Hyperplasia Following Balloon Injury

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Background: Thrombin plays an important role in the development of restenosis and atherosclerosis after percutaneous coronary intervention using protease-activated receptors (PARs). Thrombin receptor (PAR-1), one of the PARs, mediates a variety of cellular actions of thrombin such as smooth muscle cell (SMC) proliferation and platelet aggregation. We succeeded in developing an orally active PAR-1 antagonist, E5555. The aims of this study is to clarify the in vitro profile of E5555 and to evaluate the effect of E5555 on intimal hyperplasia after balloon injury of the rat carotid artery.

Methods: 1) Human platelet membranes were incubated with [3H]high-affinity thrombin receptor activating peptide (TRAP) in the presence of E5555. 2) Effects of E5555 on rat SMC proliferation induced by thrombin (0.1 units/mL), basic fibroblast growth factor (3 ng/mL) or platelet-derived growth factor (30 ng/mL) was evaluated by colorimetric assay using MTT. 3) E5555 (10 and 30 mg/kg) or vehicle was given orally to male rats once a day for 16 days. On day 3, carotid artery lesion was induced by balloon denudation. Fourteen days after the surgery, the injured vessels were harvested and elastia-van Gieson's staining was performed.

Results: 1) E5555 inhibited binding of [3H]high-affinity TRAP to PAR-1 in human platelet membranes in a concentration-dependent manner with an IC50 value of 0.019 µM (n=6).

2) E5555 inhibited rat SMC proliferation induced by thrombin with an IC50 value of 0.16 µM (n=4), but did not inhibit that induced by basic fibroblast growth factor or platelet-derived growth factor 3. The area of neointima in the vehicle-treated group (n=23) was 0.13±0.010 mm² (means±SEM), while that in the group treated with E5555 at 10 mg/kg (n=24) and 30 mg/kg (n=24) were 0.116±0.007 mm² (ns vs. vehicle) and 0.078±0.009 mm² (p<0.001), respectively. The ratio of neointimal to medial area was significantly decreased in the group treated with E5555 at 50 mg/kg (0.866±0.092 vs. 1.404±0.091 in vehicle, p<0.001) without affecting the medial area.

Conclusion: E5555, a potent and orally active PAR-1 antagonist, may be beneficial for the treatment of restenosis after percutaneous coronary intervention.