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

Klaus Pels, Carolin Deiner, Ursula Rauch, Christoph Loddenkemper, Peter Lothar Schwimmeck, Charite-University Medicine Berlin, Campus Benjamin Franklin, Berlin, Germany

BACKGROUND: Prolonged Clopidogrel therapy after intracoronary radiation (IR) treating 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+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 ionizing radiation 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 was administered one hour prior to euthanasia to label proliferating cells. Coronary arteries were immunohistochemically examined 3 months after injury. RESULTS: Cell proliferation was significantly reduced in the 28dCl group compared to the 90dCl group (PTCA: 18.40 ± 2.17 proliferating cells/mm² in the 90dCl group vs. 8.82±0.9 and 9.8±3.1/mm² in the control group; p<0.05). Total plaque volume percent (=vessel-lumen volume/vessel volume%) at non-stented sites, at baseline and follow-up, was: S: 53±9 and 39±9%, and P: 51±12 and 57±11% (p<0.05). External plaque volume percent (=vessel-lumen volume/stent length), at baseline and follow-up, was: S: 11.9±4.2 and 7.9±3.3/mm³, and P: 10.9±4.0 and 11.6±3.5/mm³ (p<0.05). Total plaque percent (=vessel-lumen volume/vessel volume%) at stented site, at baseline and follow-up, was: S: 5.7±1.4 and 6.1±2.2 mm² (p<0.05); neointimal volume index (=stent-lumen volume/stent length) was: S: 3.6±1.8 and P: 3.8±2.3 mm²/mm³ (p<0.05); obstruction volume percent (=stent-lumen volume/stent volume%) was: S: 34±15 and P: 35±23% (p<0.05). External plaque percent (=vessel-lumen volume/vessel volume%) at stented site, at baseline and follow-up, was: S: 53±10 and 39±9%, and P: 51±12 and 57±11% (p<0.05). External plaque volume index (=vessel-lumen volume/stent length), at baseline and follow-up, was: S: 11.9±4.2 and 7.9±3.3/mm³, and P: 10.9±4.0 and 11.6±3.5/mm³ (p<0.05). Total plaque percent (=vessel-lumen volume/vessel volume%) at stented site, at baseline and follow-up, was: S: 53±10 and 39±9%, and P: 51±12 and 57±11% (p<0.05).

CONCLUSION: In normocholesterolemic patients, prolonged treatment with oral simvastatin shows no effect in preventing ISR and neointimal growth after coronary stenting. However, it reduces MACE and induces a diffuse regression of the atherosclerotic plaque burden.

9:45 a.m.

884-6

Effect of Percutaneous Transluminal Renal Artery Angioplasty With Stenting on Renal Function in Patients With Atherosclerotic Renal Artery Stenosis

Johan D. Asaas, David S. Bromet, Roy P. Venzon, Stamatis Dimitropoulos, Martha Gulati, Clifford J. Kavinsky, Gary L. Schaer, Jeffrey R. Snell, Rush University Medical Center, Chicago, IL

Background: Atherosclerotic renal artery stenosis (ARAS) is a known risk factor for renal failure. Percutaneous transluminal renal artery angioplasty with stent placement (PTA-S) is used to treat ARAS. Whether PTRA-S slows down or reverses the deterioration of renal function remains controversial. A retrospective review of 80 consecutive patients with ARAS who underwent PTRA-S at our institution was performed to determine the effect of PTRA-S on renal function.

Methods: All patients with ARAS who underwent PTRA-S at our institution from 7/97 to 7/02 were included in our review. Serum creatinine (SCr) levels were followed for 4 years (2 years prior to and 2 years post PTRA-S). 1/SCr was used to approximate renal function. Linear regression analysis was done to determine the best-fit slope of renal function over time.

Results: 98 PTRA-S procedures were performed on 80 patients with ARAS. In the 24 months prior to intervention, there was a statistically significant decline of renal function: slope of -0.005 [P=0.005, 95% CI (-0.007, -0.003)]. Post intervention renal function significantly improved: slope of +0.0024 [P<0.019, 95% CI (0.001, 0.004)]. This reversal of the decline of renal function was sustained over the two years post intervention.

Conclusion: This study demonstrates that PTRA-S reverses the decline in renal function seen in patients with ARAS. These findings have important clinical implications.

11:00 a.m.

887

Peripheral Intervention: Renal and Carotid

Wednesday, March 10, 2004, 10:30 a.m.-Noon Morial Convention Center, La Nouvelle B

10:30 a.m.

877

Endovascular Gamma Radiation Therapy Inhibits Recurrence in Restenotic Lesions of the Femoropopliteal Artery: The Vienna Experience

Roswita M. Wolfgram, Erich Minar, University of Vienna, General Hospital Vienna, Vienna, Austria

Background: Intracoronary gamma radiation therapy efficiently improves freedom from recurrent disease in patients with restenosis. This retrospective analysis was designed to evaluate the efficacy of the gamma emitter 192Ir for the prevention of recurrent re-stenosis in the femoropopliteal arteries in patients treated for restenosis.

Methods and Results: A total of 197 patients, treated with either radiation (N=100) or placebo therapy (N=97), for de-novo or recurrent disease, were retrospectively analyzed. Sixty-six patients with de-novo-, and 34 patients with recurrent lesions were treated with gamma radiation. The outcomes of those patients were compared to outcomes of 67 patients with de-novo-, and 30 patients with recurrent lesions treated with percutaneous transluminal angioplasty (PTA) alone. At 6-, and 12-months there was no difference for the incidence of restenosis in the de-novo group. In patients initially treated for recurrence, however, 6-, and 12-months restenosis rates were significantly lower in the radiation versus the PTA alone group (6-months: 20.7% versus 66.7%; p<0.001, 12-months: 26.5% versus 47.8%; p<0.001).

Conclusion: The combined therapy of PTA and gamma radiation with 192Ir, for patients with recurrent disease in the femoropopliteal arteries results in significant reduction of restenosis at 6 and 12-months, but does not impact on restenosis in patients with de-novo lesions.

10:45 a.m.

877-2

Recurrence in Restenotic Lesions of the Femoropopliteal Artery: The Vienna Experience

Roswita M. Wolfgram, Erich Minar, University of Vienna, General Hospital Vienna, Vienna, Austria

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11:00 a.m.

877-3

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Roswita M. Wolfgram, Erich Minar, University of Vienna, General Hospital Vienna, Vienna, Austria

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