

POSTER SESSION

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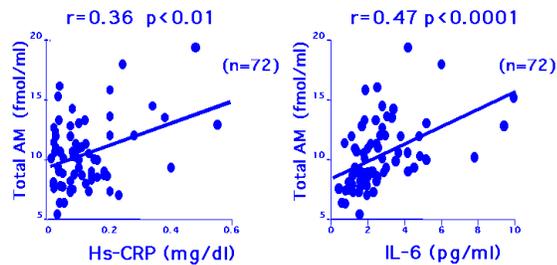
Aortic and Peripheral Arterial Diseases

Monday, March 08, 2004, 9:00 a.m.-11:00 a.m.
Morial Convention Center, Hall G
Presentation Hour: 9:00 a.m.-10:00 a.m.

1066-189 Elevation of Plasma Adrenomedullin Level Is Closely Related to C-Reactive Protein and Interleukin-6 in Patients With Peripheral Arterial Occlusive Disease

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Background: Adrenomedullin (AM) is known to have anti-atherosclerotic and anti-inflammatory effects. Although previous studies have shown that plasma AM levels are elevated in various diseases, there are no data about its level in patients with peripheral arterial occlusive disease (PAOD), one of severe atherosclerotic diseases. **Methods and Results:** We examined 33 patients with PAOD and 39 patients without PAOD. Between the two groups, there was no significant difference in clinical and laboratory parameters except serum creatinine and ankle brachial index (ABI). The plasma AM concentration in PAOD group was significantly higher than in non-PAOD group (11.5 ± 3.0 vs. 9.5 ± 2.2 fmol/mL, $p < 0.01$). Its level had a correlation with the severity of PAOD, i.e., with ABI ($r = 0.39$, $p < 0.01$) and Fontaine classification ($r = 0.32$, $p < 0.01$). Furthermore, plasma AM was significantly correlated with C-reactive protein and interleukin-6 (figure). By multiple regression analysis, ABI and IL-6 were independent determinants of the plasma level of AM. **Conclusions:** The plasma AM concentration was elevated in patients with PAOD in proportion to the severity. The AM level was also associated with CRP and IL-6, markers of inflammation. Recent studies showed that elevation of inflammatory parameters, such as CRP and IL-6, was strongly related to future cardiovascular events. Therefore, an increased production of AM in patients with PAOD may play a protective role against advanced atherosclerosis with inflammatory signature.



1066-190 Influence of Statin Therapy on Arterial Elasticity in Essential Hypertension

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Background: The vascular remodeling is a common problem in patients (pts) with arterial hypertension (HA). Statins by influence on migration and proliferation of smooth muscle cells may inhibit the posthypertensive arterial remodeling. Pulse wave velocity (PWV) provides an indirect, non-invasive measurement of the mechanical properties of arteries. The aim of the study was to evaluate the influence of statins on arterial elasticity in HA. **Methods:** The study group consisted of 52 pts with essential moderate HA. They were randomised into Group I (26 pts who received statin) and Group II (26 pts who received placebo). Groups were comparable according to age, gender, blood pressure values and treatment of HA. Before and following 6 months of treatment PWV was evaluated using a computer system COMPLIOR. For automatic measurement of PWV pressure waveforms were digitized at rate 500 Hz for carotid-femoral distance. 10 healthy volunteers constituted a control group.

Results: After 6 months similar reduction of BP was observed in both groups. Following 6 months of conventional treatment of HA the PWV was slightly decreased. Addition of statin caused the significant reduction of PWV. ($*p < 0.01$)

Conclusions: 1. Addition of statin to conventional treatment may improve arterial elasticity in essential HA.

2. Statins are likely to inhibit posthypertensive arterial remodeling

PWV in m/s

	Group I	Group II	Control
Initial	13,2 +/- 1,8	12,9 +/- 1,6	7,0 +/- 0,6
After 6 months	8,1 +/- 0,7 *	10,3 +/- 1,1	7,2 +/- 0,4

1066-191

A Phase I Study of Intramuscular Administration of Plasmid, Developmentally Regulated Endothelial Cell Locus-1 Gene, in Humans With Peripheral Arterial Disease

Sanjay Rajagopalan, Jeffrey Snell, Marc Litt, Gary L. Schaer, Ronald Karlsberg, Suheil Dohad, Stuart W. Young, Valentis Inc., Burlingame, CA

Background: Developmentally regulated endothelial locus 1 (Del-1) is a novel angioma-trix protein. Preclinical studies using a plasmid expressing Del-1 (VLTS-589) in conjunction with a poloxamer have demonstrated functional improvements in lower extremity perfusion and exercise tolerance. The objective of this investigation was to assess the safety of VLTS-589 in subjects with peripheral arterial disease (PAD).

Methods: Subjects with either intermittent claudication (Rutherford 2 and 3, n=18) or critical limb ischemia (resting pain, Rutherford 4, n=9) were enrolled in an open-label, dose escalation, 90 day follow-up study after exclusion of conditions that may preclude angiogenic growth factor delivery (malignancy, retinopathy etc.). 27 subjects received IM injections in 1 lower extremity (3 to 84 mg, 7 cohorts, C1-C6b; circumferential [C6a] and posterior, linear [C6b] pattern of injections).

Results: There were no serious adverse events attributable to VLTS-589; no subjects required amputation. Transient ecchymosis at the injection site, noted in 4 subjects, was attributed to the injection procedure. Changes in mean peak walking time (PWT) for subjects able to exercise and Ankle/Brachial Index (ABI) data for the entire cohort is reported below in Table 1.

cohorts	1 3 mg	2 6 mg	3 12 mg	4 36 mg	5 60 mg	6a 84 mg	6b 84 mg
pABI	.02	.12	.13	.18	.07	.02	0.03o;p>
pPWT (min)	.10	.57	.84	.87	.63	.0	SPAN style="FONT-SIZE: 9pt; mso-bidi-font-size: 10.0pt">0.73
Change PWT	6	1	3	99	24	7	8

Conclusion: IM delivery of up to 84 mg VLTS-589 is well tolerated. These data supported a controlled Phase II clinical trial (DELTA-1 or Del-1 for Therapeutic Angiogenesis), which is currently in progress.

1066-192

Effect of Enzyme Replacement Therapy on Intima Media Thickness and Endothelial Function in Fabry Disease

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Background: Fabry disease is an inborn lysosomal storage disorder with deposition of glycosphingolipids in the vascular system including endothelial- and smooth muscle cells, possibly leading to endothelial dysfunction. We tested the hypothesis whether enzyme replacement therapy (ERT) with agalsidase would alter vascular function.

Methods: Flow mediated vasodilatation (FMD) of the radial artery was assessed using high-resolution ultrasound; nitroglycerine (NG) sublingually induced endothelium independent vasodilatation. Results are expressed as percent change of diameter from baseline. Intima-media thickness of the brachial artery (IMT) was calculated with a vessel wall detection software.

Results: 13 hemizygote and 10 heterozygote patients were compared before and after 0.9 years of ERT to 15 age and risk factors matched healthy subjects. Hemizygote Fabry patients presented with greater IMT at baseline compared to control and heterozygote patients ($470 \pm 34 \mu\text{m}$ vs. $401 \pm 13 \mu\text{m}$ and $402 \pm 10 \mu\text{m}$; $p = 0.029$ and $p = 0.049$); FMD in hemizygote and to a less extent in heterozygote patients tended to be impaired versus control ($5.4 \pm 0.9\%$ and $6.1 \pm 0.9\%$ vs. $8.2 \pm 1.2\%$; $p = 0.09$ and $p = 0.19$). ERT led to normalisation of IMT in hemizygote patients ($397 \pm 12 \mu\text{m}$; $p = 0.05$) but had no effect on endothelial function ($5.0 \pm 1.2\%$; $p = 0.7$). IMT correlated inversely with FMD in the control group ($r^2 = 0.411$), but not in Fabry patients ($r^2 < 0.01$).

Conclusions: One year of ERT reduced IMT in hemizygote patients but had no effect on endothelial function. Our data suggest that structural changes seen in Fabry disease are unrelated to functional parameters as typically observed in atherosclerotic vascular disease.

1066-193

Endovascular Stent-Graft Placement for Nonsurgical Repair of Descending Aortic Perforations: Acute and Follow-Up Results

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Background: Perforating lesions of the descending thoracic aorta are a life-threatening condition associated with high morbidity and mortality.

Methods: Between January 1999 and October 2002 a total of 25 consecutive patients (15 male, mean age 63.3 years) underwent percutaneous treatment for perforating lesions in the descending aorta. In 19 cases (group A) the aortic perforation was due to ruptured aortic type-B dissections (n=13) or rupture of preexisting atherosclerotic thoracic aneurysms (n=6); 6 patients (group B) were treated for posttraumatic perforations of the descending aorta. In total 31 endoprostheses were implanted (4 patients with two and 1 patient with three endoprostheses).

Results: The implantation of the endoprosthesis was successfully performed in all cases without periinterventional complications. In one case implantation of a second endopro-