Atorvastatin mediates pleiotropic effects in hypercholesterolemic patients via the Renin-Angiotensin-System (RAS) by increasing Angiotensin-(1-7)

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Aim: The present study was undertaken to investigate if atorvastatin exerts RAS-inhibiting effects and modulates vascular responsiveness in severely hypercholesterolemic patients. Irbesartan was used as a positive control.

Methods: A 12-week study was conducted in a randomized, double-blind crossover design. 12 severe hypercholesterolemic patients were randomized to receive 40 mg atorvastatin and after washout, 150 mg irbesartan per os daily for another month. Venous responses to Ang II, histamine and glyceroltrinitrate were compared before and after each treatment using the dorsal hand vein compliance method. Plasma levels of Ang II and the pleiotropic peptide Ang-(1-7) were determined before and after each treatment using a radioimmunoassay (RIA). Pulse wave velocity was additionally measured as surrogate parameter for arterial elasticity using the AtCorMedical Sphygmocor device.

Results: Ang II-induced constriction was significantly reduced to 38±8% basal vein size [BVS] after atorvastatin compared to 29±7% before treatment (p=0.04). Correspondingly, Ang II-induced constriction was 40±11% before versus 64±8% BVS after irbesartan treatment (p=0.07). Ang II plasma levels increased only after irbesartan treatment from 17±6 to 52±12 pg/ml (p=0.048) compared to atorvastatin: 9±1 versus 11±3 pg/ml, whereas plasma levels of the pleiotropic RAS-peptide Ang-(1-7) increased from 24±2 to 32±2 pg/ml after atorvastatin (p=0.023) compared to 18±3 before versus 37±4 pg/ml after irbesartan (p= 0.002). Pulse wave velocity was slightly reduced after atorvastatin (7.0±0.4 before versus 6.8±0.4 m/s; p=n.s.) and significantly reduced from 6.9±0.4 m/s before compared to 6.3±0.3 m/s after irbesartan treatment (p=0.046).

Conclusion: Increased plasma levels of the pleiotropic peptide Ang-(1-7) after atorvastatin treatment indicate a RAS-inhibitory effect of the statin in patients with lipometabolic disorders which might contribute to its beneficial antiatherosclerotic effects.

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