Losartan ameliorates diabetic vascular hyper-reactivity to angiotensin II by reducing ROCK1 expression and activity
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We investigated the effect of an in vivo treatment with losartan, an angiotensin type I receptor antagonist (ARB), on the angiotensin II (ATII) contracture elicited in phenylephrine pre-contracted aortic strips isolated from normo (groups A and B) and hyperglycemic rats (STZ injected, 55 mg/kg; group C and D) not treated (groups A and C) and treated with losartan (20 mg kg⁻¹ day⁻¹; groups B and D). While ATII showed similar E50 values in all the preparations tested, its maximum effect (expressed as % of maximum phenylephrine contraction) reached 360% in group C, 250% in group D and only 175% in groups A and B. Aortas from all the animal groups responded similarly to irbesartan, an ARB, added to superfusion medium (50% reduction of the ATII maximum effect). The ATII contracture in groups C and D were reduced (32% and 22% respectively) by fasudil, an inhibitor of the RhoA/ROCK1 pathway. Exposure to the same drug left unchanged the ATII contracture in the aortas from groups A and B. ROCK1 enzyme activity (mU/mg of tissue proteins) was 0.04 ± 0.01 in normoglycemic, 1.42 ± 0.22* (p < 0.001 vs. groups A and B) in diabetic aortas and only 0.72 ± 0.05$ (p < 0.05 vs. groups A and B) in the aortas from losartan-treated diabetic rats.

In diabetes, ROCK1 overexpression is functionally coupled with aorta hyper-reactivity towards ATII. We provide evidence stating that losartan ameliorates vascular response to ATII reducing ROCK1 activity and expression.

Keywords: Diabetes mellitus; Renin angiotensin system; Pharmacology

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Endothelium-dependent prothrombotic and fibrinolytic factors in patients with chronic heart failure
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Along with disturbance of blood flow, a hypercoagulable state, endothelium plays an important regulatory role thromboembolic pathophysiology and produces prothrombotic and antithrombotic factors in the chronic heart failure (CHF). In study we have investigated endothelial-dependent hemostasis [von Willebrand factor (vWF), tissue plasminogen activator (tPA)] and endothelial damage [circulating endothelial cells (CECs), an index of endothelial damage] in 108 patients with ischemic heart disease and CHF I–IV class (NYHA), who were compared with 30 age-matched patients with ischemic heart disease without CHF and 27 age-matched healthy control subjects.

Results: There was an increase plasma levels CECs in patients with CHF compared without CHF (p = 0.002) and healthy controls (p = 0.001). Patients with more severe symptoms CHF (class III–IV) had higher CECs (p = 0.01), vWF (p = 0.02), lower tPA-antigen (p = 0.1), than class I–II. A significant increase