DIRECT AT2 RECEPTOR STIMULATION PROTECTS AGAINST VASCULAR REMODELING IN L-NAME HYPERTENSION


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Increased pulse wave velocity (PWV) represents an independent cardiovascular risk factor and serves as a direct marker of arterial stiffness. Novel means to target pulse wave velocity are currently an attractive problem of hypertension research. Previously, the AT2 receptor (AT2R) stimulation elicited anti-inflammatory, cardioprotective and renoprotective effects. Therefore, we investigated, whether an AT2R agonist, compound 21, alone or combined with AT1 receptor blockade prevented aortic stiffening in L-NAME-induced hypertension. Male adult Wistar rats (n=65) were randomized into 6 groups: control, L-NAME, L-NAME + compound 21, L-NAME + olmesartan and L-NAME + compound 21 + olmesartan. Blood pressure (BP) was measured each week. After 6-week treatment, aortic hydroxyproline content, PWV, wall thickness (WT) and inner diameter were determined and aortic stiffness (elasticity modulus) was estimated. L-NAME administration was associated with augmented BP, PWV, WT and stiffness increase and partly prevented hydroxyproline accumulation. Olmesartan completely prevented BP, PWV, WT and stiffness increase and partly prevented hydroxyproline accumulation. Compound 21 partly prevented all these alterations, yet without concomitant prevention of BP rise. Although the combination therapy with olmesartan and compound 21 led to BP levels, PWV and WT comparable to olmesartan alone-treated rats, only in the combination group complete prevention of increased hydroxyproline deposition was achieved, resulting in even more pronounced stiffness reduction. We conclude that in rats with inhibited NO-synthase, the BP-independent effect on aortic stiffening and collagen accumulation by AT2R stimulation was additive to AT1 receptor blockade. (Partly supported by APVV-0205-11 and VEGA-1/0831/11)