Angiotensin II Receptor Type 1 Blockade Prevents Arterial Remodeling and Stiffness in Iron Overloaded Rats

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Introduction: Iron is an essential metal for cellular homeostasis participating in important physiological processes. Concentrations of this metal in the organism need to be rigorously regulated, because the deficiency and excess of this metal cause serious damage to health. Regarding iron overload, it has been suggested that the vasculature is damaged human and animal models, characterized by endothelial dysfunction and reduced compliance.

Objective: To prove that angiotensin II receptor type 1 blockade prevent arterial remodeling and stiffness in iron overloades rats.

Material and Methods: We previously demonstrated that in vitro blockade of the angiotensin II type 1 receptor (AT1R) reversed functional vascular changes induced by chronic iron overload. In this study the effect of chronic AT1R blocker on aorta stiffening was test in iron overloaded rats. Aortic mechanics, geometry, and composition was assessed in Wistar rats treated for 15 days with saline as control group, iron-dextran 200 mg/kg/day five days a week (iron overload group), losartan (20 mg/kg/day in drinking water), and iron-dextran plus losartan.

Results: There were no differences in aortic hemodynamics and vascular tone due to iron overload, but thoracoabdominal aortic pulse-wave velocity (PWV) increased significantly indicating a decrease in aortic compliance. Co-treatment with losartan prevented changes on PWV, β-index and elastic modulus from iron overloaded rats. This iron-related increase in PWV was not related to changes in aortic geometry and wall stress but increased elastic modulus/wall stress ratio suggesting that a change in the composition of the wall was responsible for the stiffness. Confirming, despite not changing circulating iron or vascular deposits, losartan also ameliorated the increase in aorta collagen content of the iron overload group.

Conclusions: Taking together, losartan prevented the structural and functional indices of aortic stiffness in the iron loading rats, suggesting a capacity for renin-angiotensin system inhibition to limit the vascular remodeling in chronic iron overload.

Keywords: iron overload; pulse wave velocity; collagen; compliance; angiotensin