Angiotensin-(1-9) reverses experimental hypertension and cardiovascular damage by inhibition of the angiotensin converting enzyme/Ang II axis

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Abstract:

Background:
Little is known about the biological effects of angiotensin-(1–9), but available evidence shows that angiotensin-(1–9) has beneficial effects in preventing/ameliorating cardiovascular remodeling.

Objective:
In this study, we evaluated whether angiotensin-(1–9) decreases hypertension and reverses experimental cardiovascular damage in the rat.

Methods and results:
Angiotensin-(1–9) (600 ng/kg per min for 2 weeks) reduced already-established hypertension in rats with early high blood pressure induced by angiotensin II infusion or renal artery clipping. Angiotensin-(1–9) also improved cardiac (assessed by echocardiography) and endothelial function in small-diameter mesenteric arteries, cardiac and aortic wall hypertrophy, fibrosis, oxidative stress, collagen and transforming growth factor type β – 1 protein expression (assessed by western blot). The beneficial effect of angiotensin-(1–9) was blunted by coadministration of the angiotensin type 2(AT2) receptor blocker PD123319 (36 ng/kg per min) but not by coadministration of the Mas receptor blocker A779 (100 ng/kg per min). Angiotensin-(1–9) treatment also decreased circulating levels of Ang II, angiotensin-converting enzyme activity and oxidative stress in aorta and left ventricle. Whereas, Ang-(1–9) increased endothelial nitric oxide synthase mRNA levels in aorta as well as plasma nitrate levels.

Conclusion:
Angiotensin-(1–9) reduces hypertension, ameliorates structural alterations (hypertrophy and fibrosis), oxidative stress in the heart and aorta and improves cardiac and endothelial function in hypertensive rats. These effects were mediated by the AT2 receptor but not by the angiotensin-(1–7)/Mas receptor axis.

Keywords: Angiotensin II||Angiotensin-(1–9)||Cardiovascular remodeling||Fibrosis||Hypertension||Hypertrophy||Renin–angiotensin system
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