Low blood pressure and low aldosterone biosynthesis in Paraoxonase 1 (PON1) knockout mice.

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Abstract

Paraoxonase 1 (PON1) is an HDL associated lipo-lactonase that has been shown in epidemiological studies to be inversely related to blood pressure (BP). We used PON1 knockout (PON1KO) mice to test the role of PON1 in BP regulation and the possible association with the renin-angiotensin-aldosterone system. In PON1KO mice, systolic and diastolic BPs were both lower, by 14.8 and 10.9 mmHg, respectively, compared to control, C57 mice ($p<0.001$). Plasma renin activity was similar in PON1KO and in C57 mice (51.09±17.37 and 59.69±10.47ng AngI/ml/hr, respectively), suggesting a renin-independent phenomena. However, basal serum aldosterone levels were significantly reduced by 32% in PON1KO in comparison to control mice ($p<0.05$) with no significant changes in urine or serum electrolytes. Adrenal aldosterone synthase (AS) mRNA expression was also significantly reduced. Plasma angiotensin II was also lower in PON1KO mice (720 compared to 1100 pgr/ml in C57 mice). When challenged by low -salt diet (LSD), BP was further reduced in PON1KO mice as compared to C57. Administration of angiotensin II did not increase BP or aldosterone but it enhanced AS expression. Addition of 3% KCl in the drinking water increased both, BP and aldosterone to a level similar to C57. Administration of aldosterone did not change BP in PON1KO mice. Manipulation of vascular relaxation, using nitric oxide synthase inhibitor, resulted in increased BP but had no effect on serum aldosterone level.

In conclusion, the present study shows that PON1 regulates BP and aldosterone biosynthesis but these two observations have no causal relationship. Further studies are needed to elucidate the exact mechanism by which PON1 exerts its effects.