Cardioprotective Effects of Paraoxanase 3 in a Dahl Salt-Sensitive Rat Model of Chronic Kidney Disease

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Objective: Paraoxanases (Pon) are hydrolytic enzymes with three distinct isoforms. Decreased circulating Pon activity is associated with increased oxidant stress and adverse clinical outcomes in the setting of chronic kidney disease (CKD), yet the mechanism of action is unknown. We tested the hypothesis that Pon-3 is cardioprotective in a Dahl salt-sensitive model of hypertensive renal disease.

Methods: Ten week old, age-matched, Dahl salt-sensitive wildtype and Pon3 mutant male and female rats were maintained on eight percent high salt diets for eight weeks to initiate the salt-sensitive hypertensive renal disease characteristic of this model. After eight weeks, animals were euthanized and hearts were processed for histology. Echocardiography was performed to measure left ventricular function.

Results: By 8 weeks, mortality was observed in 18.2% of male SS-Pon3 KO rats on high salt; no mortality was observed in male SS male rats on high salt. In female rats, by 8 weeks 100% mortality was observed in SS-Pon3 KO rats on high salt diet while no mortality was observed in SS rats on high salt. High salt fed SS-Pon3 KO male rats that survived the echocardiography study demonstrated significantly decreased left ventricular end-systolic diameter and end-diastolic diameter, as well as significant increases in left ventricular relative wall thickness compared to age matched SS rats. Furthermore, SS-Pon3 KO rats demonstrated significantly increased heart-weight-to-body-weight ratio compared to age matched SS rats.

Conclusion: These findings suggest a cardioprotective role for PON-3 in the setting of salt-sensitive hypertensive renal disease.

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