Maintaining Normal Blood Pressure in a Renovascular Stenosis Model of Hypertension in Adult Lewis Rats: Putative Physiological Modulation of the Renin-Angiotensin System

Prolonged unilateral renal artery stenosis using a Goldblatt Two-Kidney-One Clip (2K1C) technique is a validated scientific approach to inducing experimental hypertension in laboratory animals. This patho-physiological modulation is associated with the activation of the renin-angiotensin system with increased renin and angiotensin II release to initiate hypertension. This mode of experimental hypertension has been demonstrated for many rat strains including Sprague Dawley, Brown Norway and Wistar Kyoto but has not been fully characterized in syngeneic Lewis rats. The objective of this study was to develop and characterize a unilateral renal artery stenosis model of hypertension in adult male Lewis rats using a 2K1C method for hypertension studies in our laboratory. Thirty animals were randomly assigned to two groups to undergo sham or the 2K1C surgical procedure under isoflurane-induced anesthesia; approval was granted by our institutional animal ethics committee (A2404, n =15 per group). Hemodynamic parameters including heart rate; systolic and diastolic blood pressure were monitored weekly for 6 weeks, using a volume-pressure tail cuff and a CODA pressure computer. Plasma concentrations of critical biomarkers of the renin-angiotensin system were quantified using standard ELISA assays and renal histopathological changes were assessed microscopically. Unilateral renal arterial stenosis caused marked renal atrophy, glomerulosclerosis and interstitial fibrosis, but a compensatory renal hypertrophy was observed in contralateral kidneys. Interestingly, unilateral renal arterial stenosis failed to induce hypertension over the six week period. The resistance to develop hypertension in the 2K1C group was associated with a significant decrease in total plasma renin (P = 0.023), an increase in the ratio of plasma angiotensin (1-7) to total renin (P = 0.034) and a decrease in the ratio of angiotensin II to total renin (P = 0.013). There were no changes in plasma electrolytes, glucose, creatinine or urea. These data demonstrate that adult male Lewis rats may have physiologically modulated the activation of the renin-angiotensin system to maintain a homeostatic balance and resist hypertension following unilateral renal artery stenosis.