A NOVEL ATRIAL NATRIURETIC PEPTIDE BASED THERAPEUTIC IN EXPERIMENTAL ANGIOTENSIN II MEDIATED ACUTE HYPERTENSION

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Studies were performed in normal male mongrel dogs (21–27 kg) on a fixed sodium diet (58 mEq/day, Hill's ID, Topeka, KS) with free access to drinking water. The night before experimentation, dogs were fasted and given 300 mg of lithium carbonate for assessment of renal tubular function. Dogs were anesthetized with pentobarbital sodium (15 mg/kg intravenous), intubated, and mechanically ventilated with supplemental oxygen (Harvard respirator, Amersham, MA) at 12 cycles/min. A balloon-tipped thermodilution catheter was advanced to the pulmonary artery via the external jugular vein for measurement of cardiac filling pressures [pulmonary capillary wedge pressure (PCWP), pulmonary artery pressure (PAP), and right atrial pressure (RAP)] and cardiac output (CO). The femoral artery was cannulated for MAP monitoring and blood sampling. The femoral vein was cannulated for inulin, ANG II, and M-ANP or normal saline or BNP infusion. The left kidney was exposed and the ureter was cannulated for urine sampling. An electromagnetic renal artery flow probe (Carolina Medical Electronics, East Bend, NC) was used to measure renal blood flow (RBF). Systemic vascular resistance (SVR), pulmonary vascular resistance (PVR), and renal vascular resistance (RVR) were calculated as (MAP-RAP)/CO, (PAP-PCWP)/CO, and (MAP-RAP)/RBF respectively. Supplemental non-hypotensive doses of pentobarbital were administered as needed. After completion of the above procedural set up a weight-adjusted inulin bolus was administered followed immediately by continuous inulin infusion to maintain plasma inulin levels between 40 and 60 mg/dL for determination of GFR. The experiment began after a 60 minute equilibration period.