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BNP-32 LEVELS CORRELATE WITH PULMONARY HYPERTENSION PROGRESSION IN RATS
Palaniswamy Vijay, Thomas G. Sharp, John W. Brown, Surgery, Indiana University School of Medicine, Indianapolis, IN.

Objective: Pulmonary hypertension is a progressive disease that leads to right heart failure and eventually death. Brain natriuretic peptide (BNP) has been shown to be a marker for severity of heart failure. In this study, we studied the dynamic changes of BNP during the progression of chemically induced pulmonary hypertension in rats.

Methods: Male Sprague Dawley rats (200-250gm) were injected with 60mg/kg/b.wt monocrotaline (MCT) in saline. Control rats received saline alone. The rats were terminated 7, 14 and 21 days after the treatment and their plasma BNP-32 (ng/ml) was determined. There were at least eight in control and 10 rats in MCT group per time point.

Results: At the end of 21-day induction of pulmonary hypertension, four male rats died due to right heart failure. The levels of BNP increased significantly with time and differed from control male rats. BNP levels in control rats were 0.45±0.03ng/ml. The data are given in the table below. The levels were 0.82±0.1, 2.47±0.08, and 4.81±0.2ng/ml in rats terminated 7, 14, and 21 days post MCT-treatment. All the levels were significant at a p-value of 0.001. The rats that died on day 21 had plasma levels of 11.93±0.1ng/ml, 3 times the levels of surviving rats at the same time point.

Conclusion: Pulmonary hypertension damages pulmonary vasculature that causes release of vasoconstrictive mediators that leads to right heart failure. This failure results in ventricular hypertrophy and death. The marker of heart failure, BNP-32 is elevated with the progression of disease that could be clinically used to identify the severity of the disease in surgically-induced secondary pulmonary hypertension.

Key Words: BNP, Pulmonary Hypertension

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INTERLEUKIN-6 GENE -573G>C PROMOTER POLYMORPHISM IS ASSOCIATED WITH PLASMA FIBRINOGEN LEVEL AND HYPERTENSION IN HONG KONG CHINESE
Louisa YF Wong, Yu-Bun Man, Raymond YH Leung, Bernard MY Cheung, Department of Medicine, The University of Hong Kong, Hong Kong, China.

Inflammation is an important mechanism in cardiovascular disease. Interleukin-6 (IL-6) is the major regulator of acute phase protein synthesis1 and plays important roles in the pathogenesis of cardiovascular disorders. Elevated IL-6 levels are associated with the development and severity of coronary disease as well as the transition to plaque instability and subsequent poor outcome in atherosclerotic processes. Several single nucleotide polymorphisms (SNPs) in the IL-6 gene promoter have been reported, of which the -174G>C has been shown to influence the basal level of circulating IL-6 in vivo and endothelial function in healthy subjects. We sought to study IL-6 gene promoter polymorphisms in the Hong Kong Chinese and determined their association with hypertension and plasma fibrinogen levels. SNPs in the IL-6 gene promoter was identified by direct sequencing of a 945-bp segment of the 5'-flanking region of IL-6 gene in which most known SNPs are located in 40 Hong Kong Chinese subjects [20 subjects with a history of ischemic heart disease (IHD) or stroke, and 20 normal controls]. Large-scale screenings of the identified SNPs were performed in 111 essential hypertensives and 118 sex and age-matched normotensive controls, using the Sequenom genotyping platform. Plasma levels of acute phase proteins were determined. A major SNP, -573C>G (rs1800796) polymorphism was found in our population (-573G allele frequency 0.24). The genotypes of -573C>G polymorphism were in Hardy-Weinberg equilibrium (p=0.92). The -174G>C and -598G>A polymorphisms, which are present in Caucasians, were almost 100% homozygous in our population. Subjects with -573G allele (CG+GG genotypes) had a higher blood level of fibrinogen than with CC (3.12±0.05 vs. 2.92±0.06, p=0.018). The -573G allele was also found to be associated with hypertension (P=0.047). In conclusion, our results raise the possibility that IL-6 gene might play a role in the pathogenesis of hypertension.

Key Words: Fibrinogen, Interleukin-6, SNP

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BENZAEPRL COMBINED WITH EITHER AMLODIPINE OR HYDROCHLOROTHIAZIDE IS MORE EFFECTIVE THAN MONOTHERAPY FOR BLOOD PRESSURE CONTROL AND PREVENTING END ORGAN INJURY
Ming-Sheng Zhou, Edgar A Jaimes, Leopoldo Raulji. Nephrology/Hypertension Section, VA Medical Center and Vascular Biology Institute, University of Miami School of Medicine, Miami, FL.

ALLHAT, a hallmark clinical trial, demonstrated that an angiotensin converting enzyme (ACE) inhibitor, a calcium channel blocker (CCB) and a diuretic similarly controlled blood pressure (SBP) and prevented end organ injury. However, in ALLHAT over 40% of patients required two or more antihypertensive medications to achieve SBP goal and concomitantly reduce end organ injury, and 12% of patients on the diuretic developed hyperglycemia. We studied the effect upon SBP and end organ injury [left ventricular hypertrophy (LHV), proteinuria and endothelium dependent relaxation (EDR) to acetylcholine (ED50)] of hydrochlorothiazide (HCTZ), the ACE inhibitor benazepril (Ben), the CCB amlodipine (Aml) or the combination of Ben/Aml or Ben/HCTZ in hypertensive Dahl salt sensitive (DS) rats. DS rats were fed normal (0.5% NaCl, NS) or high (4% NaCl, HS) salt diet for 6 weeks. HS rats developed hypertension and significant end organ injury (table). Mono- therapy with HCTZ (75 mg/L in drinking water) or Aml (10 mg/kg/day, by gavage) reduced SBP as well as proteinuria; Ben (40 mg/kg/day, by gavage) reduced proteinuria without significantly reducing SBP. In HS rats, only HCTZ reduced LHV, whereas EDR was improved by Aml and by Ben but not by HCTZ. Combination therapy of Ben with either Aml (40/10) or HCTZ (40/75) dramatically reduced SBP and end organ injury (table). These data clearly support clinical studies suggesting that combination therapy is more effective in SBP control and prevention of end organ injury as compared with monotherapy, because the mechanism of action of the different agents are complementary.

Key Words: Angiotensin Converting Enzyme Inhibitor, Calcium Channel Blocker, Salt-Sensitive Hypertension