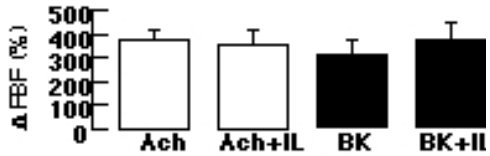
uncertain. Furthermore, there is no evidence that triglycerides or free fatty acids directly impair vascular function as opposed to reflex or hormonal changes induced following systemic exposure.

Methods: We tested the hypothesis that local HTG impairs resistance vessel endothelial function, by examining whether forearm blood flow (FBF) responses to intra-arterial acetylcholine (Ach), bradykinin (BK), and nitroprusside were altered by coinfusion of intralipid (IL 200 mg/min) for 90 min in 10 healthy adults; age 39±4, 7M.

Results: IL increased plasma triglycerides from 80±20 to 433±62 and free fatty acids from 0.5±0.1 to 1.9±0.2 (p=0.0003 for both). Forearm vasodilatation to Ach (p=0.83), BK (p=0.73), and nitroprusside (p=0.34) were not reduced by HTG (figure).



Conclusion: Local HTG sustained for >90 min does not impair resistance vessel endothelial function. These results suggest that resistance vessels are less susceptible to the deleterious effects of triglycerides than conduit vessels. Alternatively, the vascular effects of systemic HTG may be mediated indirectly, perhaps via hormonal or reflex mechanisms.

POSTER SESSION

1160 Hormone Intervention in Cardiovascular Disease

Tuesday, March 09, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1160-165 Angiotensin II Receptor 1 Blocker Improves Not Only Hypertension but Also Ventricular Arrhythmogenicity

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Background: Angiotensin II receptor 1 blocker (ARB) has been proven to improve cardiovascular mortality and morbidity. However, the influence of ARB on fatal arrhythmia remained unknown. The purpose of this study was to evaluate if ARB has any beneficial effect on ventricular arrhythmogenicity, and also if the effect is associated with the decrease of blood pressure.

Methods: This study consists of 69 patients (30 males, mean age 63.8±10 years) with hypertension in whom valsartan was administrated from February 2001 to May 2002. We assessed mean blood pressure (MBP), R_{V5}+S_{V1} on ECG, QT dispersion (QTD) and QTc dispersion (QTcD) before and 10 months later of introduction of valsartan administration. We also assessed correlation between the difference of QTD or QTcD before and 10 month later of the valsartan administration and the difference of MBP or R_{V5}+S_{V1} before and 10 month later of the valsartan administration.

Results: MBP (119.9±12.1mmHg vs. 101.9±10.6mmHg, p<0.0001), QTD (60.3±16.8msec vs. 47±11.3msec, p<0.0001) and QTcD (62.6±17.1msec vs. 49.3±12.6msec, p<0.0001) except R_{V5}+S_{V1} (2.62±1.09mV vs. 2.53±0.98mV, NS) significantly decreased through the study period. There was no significant correlation between the difference of QTD or QTcD before and 10 month later of the valsartan administration and the difference of MBP or R_{V5}+S_{V1} before and 10 month later of the valsartan administration.

Conclusion: QTD and QTcD decreased after valsartan administration. The decrease of QTD and QTcD did not correlate with the change of blood pressure or R_{V5}+S_{V1}. Thus, it is suggested that valsartan might have beneficial effect on ventricular arrhythmogenicity that could not be explained by the improvement of hypertension or left ventricular hypertrophy.

1160-166 C-Type Natriuretic Peptide Improves Left Ventricular Performance at Rest and During Exercise After Heart Failure

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Background. The diastolic dysfunction present at rest is exacerbated during exercise (Ex) in heart failure (CHF). C-type natriuretic peptide **(**CNP), the third member of the natriuretic peptide family with vasodilating, natriuretic, and lusitropic actions, may prevent this abnormal Ex response after CHF.

Methods. We assessed the effects of CNP on left ventricular (LV) systolic and diastolic performance at rest and during submaximum Ex (3.5-5.5 mph for 5-8 min) in 8 chronically instrumented dogs with pacing-induced CHF. Since CNP mediated its biological actions via cGMP, we also measured plasma cGMP levels in response to CNP infusion at rest before and after CHF.

Results. CNP (2 μg/kg plus 0.4 μg/kg/min, iv, 20 min) caused a similar increase in cGMP levels before (7.7±4.4 to 29.4±5.7 pmol/ml) and after CHF (27.7±4.4 to 69.4±5.7 pmol/ml). At rest, treatment with CNP produced reductions in LV end-systolic pressure (P_{ES}, 92±10.8 vs 102±12.1 mmHg), arterial elastance (E_A, 8.6±1.2 vs 12.2±1.4 mmHg/ml) and end-diastolic pressure (P_{ED}, 38.4±4 vs 43.2±6 mmHg) (p<0.05). The peak mitral flow (dV/dt_{max}, 198±59 vs 164±38 ml/sec) was also increased due to decreases in minimum LVP (LVP_{min}, 18.6±6.7 vs 23.3±6.3 mmHg) and the time constant of LV relaxation (τ, 41±7 vs 46±7 msec) (p<0.05). In addition, the slope of LV end-systolic pressure-volume relations (E_{ES}) produced by caval occlusion was also increased (5.4±0.6 vs 4.1±0.5 mmHg/ml). The LV-arterial (A) coupling (C), quantified as E_{ES}/E_A, was improved (0.68±0.20 vs 0.49±0.18) (p<0.05). The beneficial effects persisted during Ex after CHF. At matched levels of Ex, treatment with CNP tolerated Ex-induced increases in P_{ES} (ΔP= 3.3±0.2 vs 7.3±0.4 mmHg), mean LAP (ΔP= -3.2±2.6 vs 3.1±2.7 mmHg), and LVP_{min} (ΔP= -3.4±1.2 vs 1.3±1.0 mmHg) (p<0.05). With CNP, τ was much shortened (Δ= -0.6±4.0 vs 2.9±3.7 ms), and peak mitral flow was further augmented ($\Delta dV/dt_{max}$, 71±23 vs 41±12 ml/sec) (p<0.05).

Conclusion. After CHF, the generation of cGMP in response to CNP is not blunted. CNP produces arterial vasodilatation and augments LV relaxation, diastolic filling and LV arterial coupling, thus improving LV performance, both at rest and during Ex after CHF.

1160-167 Defining the Acute Cardiorenal Response to High Dose Nesiritide in Severe Experimental Congestive Heart Failure

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Background: Previous human studies report improved cardiac filling pressures and global clinical status in acute decompensated congestive heart failure (CHF) using human brain natriuretic peptide (BNP)/Nesiritide. Severe CHF however may be associated with emergence of reduced sensitivity to BNP due to receptor down-regulation, enhanced degradation or reduced renal perfusion pressure. We investigated the effects of clinical and high dose IV Nesiritide on systemic hemodynamics, renal function, and sodium excretion in severe canine CHF, hypothesizing that supraclinical doses further reduce cardiac filling pressures and enhance sodium excretion without marked hypotension.

Methods: We used an established model of pacing induced (240 bpm, 10 days) severe canine (n=7) CHF characterized by decreased cardiac output, increased cardiac filling pressures, sodium retention and neurohumoral activation. After a baseline clearance IV Nesiritide was infused with a lead in period followed by 30 minute clearances at doses of 100 (approximating doses in clinical trials) and 1000 ng/kg/min (10 fold greater than clinical trials).

Results: Clinical dosing decreased pulmonary capillary wedge pressure (PCWP) (23±1 vs 18±1 mmHg, p<0.05), pulmonary artery pressure (PAP) (31±3 vs 27±2 mmHg, p<0.05), and mean arterial pressure (MAP) (105±4 vs 87±4 mmHg, p<0.05), and tended to increase cardiac output (CO) (1.43±0.21 vs 1.91±0.39 L/min) vs baseline. High dose IV Nesiritide further deceased PCWP (17±2 mmHg, p<0.05) and PAP (25±1 mmHg, p<0.05), without further decreasing MAP, and tended to further increase CO. Importantly, glomerular filtration rate tended to increase compared to baseline (26±5 L/min) with both clinical (41±10 L/min) and high (48±15 L/min) doses of IV Nesiritide. Urinary sodium excretion tended to increase at clinical dosing (7±4 μEq/min)and significantly increased (12±6 μEq/min, p<0.05) with high dose IV Nesiritide vs baseline (2± 0.4 μEq/min) in the absence of further decreases in MAP.

Conclusion: These studies in experimental CHF suggest it may be possible to increase the dosing of IV Nesiritide, thus warranting carefully designed future human investigations in severe CHF.

1160-168 The Estrogen-Induced Alterations in Arterial Stiffness are Independent of the Non-Dipping Status but Attenuated by Progesterone in Hypertensive Postmenopausal Women

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Background: Large artery stiffness and attenuated nocturnal blood pressure (BP) fall are associated with unfavorable cardiovascular outcome, in essential hypertension. We assessed the hypothesis that the addition of progesterone and the absence of normal circadian BP variation may modify the beneficial effects of hormonal replacement therapy (HRT) on large artery distensibility in hypertensive postmenopausal women.

Methods: For this purpose, we studied aortic stiffness in 56 postmenopausal women (aged 52 years, 3.4 years after menopause) with untreated, mild essential hypertension randomized to conjugated estrogen alone (n=20), estrogen plus medroxyprogesterone (n=20) or placebo (n=16). Aortic elasticity was evaluated, non-invasively, on the basis of pulse wave velocity (PWV) measurements at baseline and at 12 weeks after treatment. At baseline, women receiving conjugated estrogen alone, underwent 24h ambulatory BP monitoring and were classified to non-dippers (defined by a reduction in the night mean systolic and diastolic BP <10% from day values) (n=7) and dippers (the remaining subjects) (n=13).

Results: In the entire study population office BP was 146/93 mmHg and left ventricular mass index was 104±26 gr/m2. The patients' groups were matched for age, time since menopause, smoking status, office blood pressure and PWV values at baseline. At 12 weeks of treatment, in women receiving estrogen alone, aortic PWV was significantly reduced (6.31 vs 6.09 m/sec, p<0.005), while in those receiving combined HRT or placebo, PWV did not change (6.32 vs 6.28 and 6.33 vs 6.30 m/sec, respectively, p=NS for both cases). Treatment with conjugated estrogen induced a significant reduction in aortic PWV in both groups of dippers and non-dippers, after 12 weeks. Furthermore, the degree of reduction in PWV did not differ in dippers (by 0.27 m/sec) and non-dippers (by