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Circulating Beta-Atrial Natriuretic Peptide in Human Coronary Artery Disease: A New Marker for Stage A Heart Failure?
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BACKGROUND: Studies have reported the presence of an antiparallel dimer form of atrial natriuretic peptide (ANP) named β-ANP in both atrial tissue and plasma of normal humans. β-ANP has been shown to be elevated in patients with severe congestive heart failure (CHF). Its biological significance is that it may have reduced cGMP enhancing actions compared to native ANP and its formation may be secondary to oxidative stress within the myocardium and plasma. To date, it is unknown whether β-ANP is elevated in patients with CAD independently of co-presence of left ventricular dysfunction (LVD) which represents Stage A of CHF. The aim of this study was to determine the concentration of β-ANP in patients with CAD. We hypothesized that plasma concentration of β-ANP is elevated in patients with CAD independently of co-existing LVD.

METHODS: We prospectively enrolled 58 subjects (33 men), average age 66 (41 to 84), with CAD referred to the Mayo Clinic Cardiac Catheterization Laboratory. Ejection fraction was obtained by echocardiography and was used as index of LV systolic function. We measured β-ANP by RIA. * indicates p<0.05 versus CAD.

RESULTS: β-ANP was elevated in CAD patients compared to normal subjects (25±4.2 CAD versus 7±0.7 normal*). When analyzed by subgroups, β-ANP tended to increase in the subgroup (n=13) with EF<50% compared with subjects with EF >50% (p=0.064). Importantly, β-ANP was significantly elevated in the subgroup with EF ≤50% as compared to normal (22±4.4 CAD vs 7±0.7 normal*). An inverse correlation was observed between β-ANP and EF (Spearmann r = -0.3219; 95% C.I. -0.539 to -0.064; p=0.006).

CONCLUSION: We report for the first time that β-ANP is elevated in patients with CAD and is inversely correlated with EF. More importantly, β-ANP is elevated in subjects with CAD and normal EF (p<0.05 versus A CHF). We hypothesized that plasma concentration of β-ANP is acutely or chronically increased by OSA, either in otherwise healthy subjects, or in subjects diagnosed with both OSA and chronic heart failure (CHF), or OSA and other cardiovascular diseases. All plasma BNP levels were measured in 23 patients with moderate to severe CHF who were otherwise either healthy (n=10) or who also had concomitant cardiovascular disease (n=13, 5 patients with both OSA and CHF, 8 patients with OSA and non-CHF cardiovascular disease). BNP was obtained on three occasions: first before sleep, then after 4 hours of untreated OSA and again in the morning, after 4 hours of effective treatment with continuous positive airway pressure (CPAP). BNP levels were also measured in 10 closely matched, normal healthy subjects at similar time points.

RESULTS: Baseline BNP levels were similar in the 10 otherwise healthy OSA subjects and the normal subjects before sleep (0.119±0.026 vs. 0.078±0.016 nmol/L, p=0.046) and were unaffected by several hours of untreated OSA and by acute CPAP treatment. BNP levels at baseline were higher, compared to controls, in 5 OSA patients with CHF (0.09±0.014 ng/mL, p<0.016) and in 8 OSA patients with other non-CHF cardiovascular diseases (31.7±11.4 pg/mL, p<0.05). These high levels of BNP remained stable during treatment, whereas plasma BNP tended to increase in the night in the OSA with CHF and the OSA with non-CHF cardiovascular disease groups, completely unaffected either by several hours of acute untreated OSA or by CPAP treatment.

CONCLUSIONS: Despite the metabolic and mechanical stresses elicited by OSA, OSA and of itself does not increase plasma BNP in otherwise healthy subjects during wakefulness. OSA does not elicit acute sleep-related changes in BNP in otherwise healthy subjects during wakefulness. In contrast, BNP is acutely and chronically increased by OSA, either in otherwise healthy subjects, or in subjects diagnosed with both OSA and chronic heart failure (CHF), or OSA and other cardiovascular diseases.

Utility of B-Type Natriuretic Peptide and ProBNP in Evaluation of Patients Receiving Natriocor Therapy (UBET Study)
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BACKGROUND: B-type natriuretic peptide (BNP) is synthesized in cardiac ventricles as a prohormone (108 amino acids) and during the release process is cleaved into the active hormone BNP (AA 77-108) and an inactive fragment proBNP (AA 1-76). We determined the effect of Natriocor (a human recombinant BNP) infusions on the concentrations of BNP and proBNP.

METHODS: Three groups of acutely decompensated congestive heart failure (CHF) patients received Natriocor (2 μg/kg iv bolus followed by a 0.01 μg/kg/min infusion) for 24, 36 or 48 hours (N = 10, 9 and 8 respectively). Serial blood samples were collected during and after the infusion. BNP (Biosite and Bayer Diagnostics) and proBNP (proBrain Natriuretic Peptide, Roche Diagnostics) were measured.