


cardiomyocyte hypertrophy is unknown. Previous study demonstrated that peroxisomal proliferator-activated receptor (PPAR)- α ligand (fenofibrate) prevents ET-1-induced cardiomyocyte hypertrophy. Though EPA is a ligand of PPAR- α , there was no study linking relationship between EPA and PPAR- α in the field of cardiomyocyte hypertrophy. The present study investigated whether ET-1-induced cardiomyocyte hypertrophy could be prevented by EPA pre-treatment with possible mechanistic insights. At day 4 of culture, neonatal rat cardiomyocytes were divided into three groups: control, ET-1 (0.1 nM) treated and EPA-pre-treated (10 μ M) ET-1 groups. 2-fold increase in cardiomyocyte surface area, 1.8-fold increase in total protein synthesis rate and an enhanced α -actinin expression in cardiomyocyte were observed after ET-1 administration and these changes were greatly prevented by EPA pre-treatment. ET-1-induced hypertrophied cardiomyocytes showed increases in ANP and BNP mRNA expression, which were also suppressed by EPA pre-treatment. Pre-treatment of EPA could also attenuate phosphorylated JNK (an important component of MAPK cascade) and c-Jun (downstream molecules of JNK) in ET-1-induced hypertrophied cardiomyocytes. PPAR- α expression and PPAR-PPRE binding activity were suppressed in ET-1 administered cardiomyocyte and this suppression was improved by EPA treatment. In conclusion, the present study showed that ET-1 could induce significant cardiomyocyte hypertrophy with hypertrophic markers upregulation, and that this remodeling was effectively prevented by EPA-pre-administration through the upregulation of PPAR- α and the suppression of phosphorylated JNK, and c-Jun.

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Higher circulatory level of endothelin-1 in hypertensive subjects screened through a cross-sectional study in rural Bangladeshi women

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Objective: Endothelins are powerful vasoconstrictor peptides that also play numerous other functions in many different organs. Endothelin-1 (ET-1) is the most abundant and important of this family of peptides in blood vessels. ET-1, a potential marker of endothelial dysfunction has been shown in hypertensive subjects. No study yet has investigated the circulatory level of ET-1 in a country from South Asia. The present study assessed circulating levels of ET-1 in subjects with or without hypertension and further examined their association with clinical and metabolic parameters. **Methods and results:** A total of 1802 rural Bangladeshi women with mean age of 44.16 years were studied using a cross-sectional survey. The prevalence of hypertension was 31.78%. Endothelin-1 levels were significantly higher in hypertensive than in non-hypertensive subjects (hypertensive vs non-hypertensive: 4.16 ± 0.32 vs. 3.00 ± 0.08 pg/ml, $p < 0.001$). After adjusting for age, ET-1 had significant positive associations with diastolic blood pressure (DBP) ($\beta = 0.039$, $p = 0.013$) and systolic blood pressure (SBP) ($\beta = 0.020$, $p = 0.006$). Unlike blood pressures, other variables

including insulin, fasting blood glucose, triglycerides, high-density lipoprotein cholesterol, body mass index, waist circumference and vascular endothelial growth factor were not associated with ET-1. Stepwise multiple regression analysis, after adjusting for age and all other potential variables revealed that SBP and DBP were independent determinants of ET-1. **Conclusions:** The correlation of ET-1 needs further investigations to define the clinical utility and predictive value of serum ET-1 levels in hypertension for South Asian population. Higher concentration of ET-1 suggests endothelial dysfunction already in mild forms of hypertension without further risk factors or cardiovascular complications in this apparently healthy population.

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Inverse correlation between systemic endothelin-1 level and pulmonary artery pressure in adult patients with uncorrected atrial septal defect

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Patients with ASD have increased pulmonary blood flow and may cause increase in pulmonary arterial pressure. Endothelin-1 (ET-1) mainly produced by pulmonary vascular endothelium and increased plasma ET-1 level has been reported in patients with left-to-right shunt. ASD is the most common congenital shunting in adult. However, no study addressed specifically for ASD and has evaluated the role of ET-1 in this congenital shunting. Therefore, we aim to correlate the peripheral ET-1 level with pulmonary arterial pressure in adult patients with uncorrected ASD. From July 2012–April 2013 we enrolled 55 ASD patients; mean age 34.5 years-old. Confirmation of ASD and the measurement for pulmonary arterial pressure (mPAP), right ventricular systolic pressure (RVSP), and pulmonary flow ratio (Qp/Qs) were performed using TTE and TEE. These measurements were previously confirmed with right heart catheterization and showed positive correlation ($r = 0.5$; $p < 0.0001$ and $r = 0.8$; $p < 0.0001$ respectively). Peripheral blood was withdrawn from brachial vein. Forty (72%) patients have left-to-right and 28% with right-to-left shunting. Mean mPAP was 40.1 ± 14.9 mm Hg; mean circulating ET-1 was 5.6 ± 2.1 pg/dl. Unexpectedly, the correlation between circulating level of ET-1 and mPAP was significantly inverted ($r = -0.452$; $p < 0.01$), and with RVSP was also significantly negative ($r = -0.405$; $p < 0.01$). Accordingly, the reduced circulating ET-1 level might be explained by the decrease in Qp/Qs ($r = 0.310$; $p < 0.05$). However, no differences of ET-1 were found between LtoR vs RtoL shunts (5.7 ± 0.36 vs. 5.3 ± 0.52 pg/dl; NS). As a conclusion, we observed inverted relationship between circulating ET-1 and mPAP that might partially be explained by the decreased in pulmonary flow. Further study to elucidate whether pulmonary derived ET-1 may play more roles in this disease is needed.

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Synchrotron radiation pulmonary micro-angiography to visualize pulmonary artery micro-vasculature for measurement of pulmonary arterial flow velocity in a high pulmonary flow rat model

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