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 μM) 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

Shamima Akter[a,b,c], Subrina Jesmin[a,b,c], Arifur Rahman[b,d], AKM Ahsan Habib[b,d], Nobutake Shimojo[a], Majedul Islam[a,b,c], Sohel Zaedi[b,c], Naoto Yamaguchi[b,c], Masao Moroi[c], Sosuke Kimura[c], Osamu Okazaki[c], Takashi Miyauchi[a], Satoru Kawano[a], Hidechika Akashi[c], Taro Mizutani[a]

[a]*Graduate School of Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan*
[b]*Health & Disease Research Center for Rural Peoples (HDRCRP), Mohammadpur, Dhaka 1207, Bangladesh*
[c]*National Center for Global Health and Medicine (NCGM), 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan*
[d]*Shahid Ziaur Rahman Medical College, Bogra, Bangladesh*
E-mail address: samimarub@yahoo.com (S. Akter)

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

Dyah Wulan Anggrahini, Lucia Krisdinarti, Anggoro Budi Hartopo, Arina Nugraheni, Hariadi Hariawan, Nahar Taufiq, Budi Yuli Setianto

Department of Cardiology and Vascular Medicine, School of Medicine Gadjah Mada University, Indonesia
E-mail address: wulan.anggrahini@gmail.com (D.W. Anggrahini)

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 cathetherization 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 inversed ($r = -0.452$;$p < 0.01$), 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 ± 0.36vs.5.3 ± 0.52 pg/dl; NS). As a conclusion, we observed inversed 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

Chiho Tokunaga[a], Shonosuke Matsushita[b], Kazuyuki Hyodo[c], Hiroaki Sakamoto[a], Kazunori Miyakawa[d], Misao Kubota[d], Akira Kobayashi[e], Kenkichi Tanioka[f], Yuji Hiramatsu[a], Yuzuru Sakakibara[a]