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TITLE: Endothelial cell activation in vascular disease mediated by hydrogen peroxide *in vitro*

PRESENTATION TYPE: General Communication

CURRENT SPECIAL INTEREST GROUP: Cardiovascular, Respiratory and Autonomic Control (CRAC)

Theme GC: Cardiac & Respiratory Physiology

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ABSTRACT BODY:

Abstract Body : The development of cardiovascular disease (CVD) is the main cause of death among chronic kidney disease (CKD) patients (1). Endothelial injury and dysfunction are critical steps in atherosclerosis, a major CVD (2). Increased production of reactive oxygen species (ROS) has been associated with the pathogenesis of cardiovascular diseases such as atherosclerosis, hypertension and heart failure (3). However, hydrogen peroxide (H_2O_2) modulates endothelial cell function by intricate mechanisms. Ambient production of O2.− and subsequently H_2O_2 at low levels, maintained via basal activity of pre-assembled endothelial NAD (P) H oxidases (4). Endothelial cells play an important regulatory role in the circulation as a physical barrier and as a source of a variety of regulatory substances. Dysfunction of the vascular endothelium is thus leading to atherosclerosis which is characterised by overexpression of adhesion molecule expression, comprising vascular cell adhesion molecule 1(VCAM1). This adhesion molecule has been found to be up-regulation in human atherosclerotic lesions.

The aim of this study is to evaluate the effect of H_2O_2 on the endothelial cells adhesion molecules expression. Primary cultures of Human Umbilical Vascular Endothelial Cells (HUVECs) will be maintained in endothelial growth medium supplemented with penicillin-streptomycin and supplement mix of fetal calf serum in a 37C humidified incubator in an atmosphere of 5% v/v CO_2. HUVECs will be treated with in the presence and absences of 50 μM of H_2O_2 for 2, 6, 12 and 24 h. Intracellular superoxide anion production in HUVECs will be detected by using p-Nitro Blue Tetrazolium (NBT) assay to demonstrate whether H_2O_2 induce the generation of superoxide anions intracellularly in HUVECs. The formation of blue formazan will be measured spectrophotometrically at 570 nm. Total RNA will be extracted from non-treated and treated cells and RNA quantity and quality will be checked by $OD_{260/280}$ measurements. VCAM-1 mRNA expression will be assessed using RT-PCR. Our results show that H_2O_2 could potentially significantly induce EC activation through increased mRNA expression of ICAM-1 adhesion molecules in cultured HUVECs. Treatment with N-acetyl cysteine (NAC) (bulk/nano form) could significantly attenuate the effect of H_2O_2 administration on adhesion molecule protein expression. This strongly suggests the role of ROS in the endothelial cell damage sustained. Future work is to find reliable methods to test endothelial function. Non-invasive studies such as brachial ultrasound testing are also needed to determine its predictive value as a potential predictor for cardiovascular disease.

Reference 1: Herzog CA, et al. Kidney international, 2011, 80(6): 572-586

Reference 2: Hadi HA, et al. Vascular health and risk management, 2005, 1(3): 183-198

Reference 3: Cai H. Circulation research, 2005, 96(8):818-822

Reference 4: Li JM, et al. Am J Physiol, Reg I, 2004, 287(5): R1014-R1030

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