e0136 ULTRASTRUCTURAL CHANGES AND EXPRESSION OF ENOS IN MYOCARDIAL CAPILLARY ENDOTHELIAL CELLS IN RATS WITH HYPERTENSION AND DIABETES MELLITUS

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Introduction The percentage of angina and cardiac dysfunction and cardiovascular events increased significantly in hypertensive diabetes mellitus compared with essential hypertension and type 2 diabetes mellitus alone. Hypertension and diabetes are often associated with cardiac microvascular abnormalities. The major cardiac microcirculation alterations are the capillary rarefaction and endothelial cell functional impairment, which may be in the development of coronary insufficiency. We presume that the more serious injury in cardiac microvascular structure and function followed by hypertensive diabetes mellitus.

Aims The purpose of the present study is to investigate ultrastructural changes and expression of eNOS in rat myocardial capillary endothelial cells as a response to hypertension with diabetes mellitus.

Methods The rat model of hypertension with diabetes mellitus (SHDM) and the rat model of diabetes mellitus (DM) alone were induced by an intraperitoneal injection of streptozotocin combined with high fat diet in spontaneously hypertensive rats (SHR) and SD rats, respectively. The groups were as follows: SD, DM, SHR, and SHDM. After 16 weeks, ultrastructure of the myocardial capillaries was examined by transmission electron microscopy and the expression of endothelial nitric oxide synthase (eNOS) was detected by immunohistochemistry.

Results Ultrastructural alterations of myocardial capillaries in SHR, DM and SHDM were oedematous endothelial cell, endothelial protrusions into lumen and narrowed /or irregular lumen respectively. These alterations indicate that cell injury was more significant in the myocardium of DM and SHDM. Thickening of basal lamina in myocardial capillaries with SHR was less considerable compared with SD (31.3±4.2 nm vs 28.6±3.6 nm, $p>0.05$), while thickening was a prominent feature of DM (46.6±5.3) nm and SHDM (51.5±4.6) nm (compared with SD or SHR, $p<0.01$). The expression of eNOS in myocardial tissue was significantly lower in SHDM than in SHR or DM.

Conclusions These results suggest that a combination of hypertension and diabetes mellitus enhanced the damage of myocardial capillaries endothelial cell ultrastructure and function more than either hypertension or diabetes mellitus alone.

e0137 ASSOCIATION BETWEEN LOCAL AND SYSTEMIC LEVELS OF INTERLEUKIN-1β AND INTERLEUKIN-10 IN CORONARY ARTERY DISEASE AND ITS CLINICAL RELEVANCE

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Objective To explore whether the systemic level of pro-inflammatory factor interleukin-1β (IL-1β) and anti-inflammatory factor IL-10 can reliably reflect their local levels at atherosclerosis lesions in patients with coronary artery disease (CAD).

Method 18 consecutive patients with stable angina pectoris (SAP), 21 consecutive patients with unstable angina pectoris/non-ST-segment elevation myocardial infarction (UA/NSTEMI), 30 consecutive patients with ST-segment elevation myocardial infarction (STEMI) and 30 health patients as control group. Systemic samples were obtained from aorta root in all patients (n=99), local samples from distal of the coronary lesion in patients with CAD (n=69), and samples from coronary sinus of 15 patients with STEMI.

Results No significant difference at systemic level of IL-1β among the four groups ($p=0.251$), increased the systemic level of IL-10 in STEMI group than the control group ($p=0.001$), and no difference between the local and the systemic level in SAP group ($p=0.864$, 0.545). In the UA/STEMI group, the local level of IL-10 was increased compared with systemic level ($p=0.043$), but no difference of IL-1β was found ($p=0.264$). The local levels of IL-1β and IL-10 were both increased compared with systemic level in the STEMI group ($p=0.003$, 0.029 respectively). The level of IL-1β in coronary sinus tended to be decreased compared with culprit lesion ($p=0.062$), but the IL-10 showed no great changes ($p=0.743$).

Conclusions The systemic level of pro-inflammatory marker IL-1β and anti-inflammatory maker IL-10 could not complete reliablyreflect the local changesin patients with CAD. These findings may promote our understanding regarding pathogenesis of CAD and implications of findings from previous clinical observations.

e0138 AT1 RECEPTOR BLOCKER VALSARTAN ATTENUATES LEFT VENTRICULAR REMODELLING AND FAILURE IN A RAT MODEL OF ADRIAMYCIN-INDUCED DILATED CARDIOMYOPATHY BY UPREGULATING THE EXPRESSION OF ANGIOTENSIN-CONVERTING ENZYME 2 AND ANGIOTENSIN-(1−7)

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Introduction Adriamycin (ADR) is an effective antineoplastic agent whose use has been limited by its cardiotoxic side effects. Angiotensin-converting enzyme 2 (ACE2) has emerged as a novel regulator of cardiac function by converting angiotensin II into angiotensin-(1−7). Studies suggest that ACE2 and Ang-(1−7) may play a critical role in the regulation of cardiac function. This study is to investigate the effect of AT1 receptor blocker valsartan on the expression of ACE2 and Ang (1−7) in a rat model of adriamycin-induced dilated cardiomyopathy.

Methods Weight-matched Adult male Wistar rats were randomly divided into three groups as follows: 1. the ADR group, in which 2.5 mg/kg of ADR was weekly injected via a tail vein for 10 weeks (n=25); 2) concomitant AT1 receptor blocker valsartan and ADR, in which valsartan was administered by daily gavage at a dose of 30 mg?kg-1?day-1(n=10); 3. the control group (n=10). Haemodynamics and echocardiographic measurements were obtained at 12 weeks after treatment. The plasma concentrations of Ang II and angiotensin (1−7) were determined by immunoradiometric assay. The expression of ACE2 in left ventricular myocardium was investigated by Immunohistochemistry. The expression of collagen in LV were investigated with Van Gieson staining techniques.

Results LV cavity dilatation was significantly attenuated in ADR-induced dilated cardiomyopathy rats given valsartan. Valsartan partially normalised LV contractile function, which was significantly reduced in ADR rat. The plasma concentrations of Ang II were higher in the ADR group than the control group ($p<0.01$), which was further increased by valsartan ($p<0.01$). The plasma concentrations of ang (1-7) was higher in the ADR group than the control group, valsartan treatment further increased the plasma concentrations of ang (1-7) by 1.5-fold ($p<0.01$). The expression of ACE2 was increased in the ADR group, and was further significantly augmented in valsartan treated rats. Myocardial fibrosis occurred significantly in ADR group, which was partly reversed by valsartan treatment ($p<0.01$).