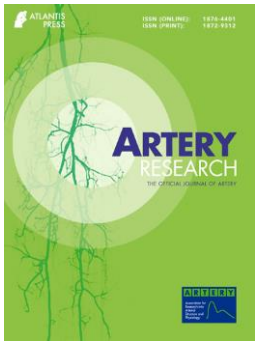

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P4.29: COMPARATIVE EFFECTS OF ANTIHYPERTENSIVE DRUGS ON OXIDATIVE STRESS AND INFLAMMATION

M. Serg, M. Zilmer, M. Zagura, J. Kals, J. Eha, K. Zilmer, T. Kullisaar, C.M. McEniery, I.B. Wilkinson, P. Kampus

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different stages of renal insufficiency (n=103, 64.8±13.3 years, 50 males, eGFR 40±21 mL/min/1.73m^2). Univariate and multiple linear regression models were used for the statistical analysis.
According to our results, logFGF23 showed significant relation with serum phosphate, PTH levels and renal function. There were no significant correlations between FGF23 and PWV or CPP. AI, however, correlated negatively with logFGF23 (r= -0.24, p<0.05). By multiple regressions, serum phosphate, logFGF23, systolic blood pressure and heart rate proved to be the individual predictors of AI. (R^2=0.31, ß=0.31, -0.33, 0.21, -0.27, p<0.05). In the subgroup of patients with <45 mL/min/1.73m^2 eGFR, serum phosphate and logFGF23 remained the significant predictors (R^2 0.21, ß=0.31, -0.39, p<0.05)
FGF23 may be a determinant of peripheral arterial elasticity independently of serum phosphate level especially in advanced stages of chronic kidney disease.
(Supported by the Hungarian Kidney Foundation and the Hungarian Society of Hypertension)

P4.27
DIABETES-EVOKED PATHOGENIC CHANGES ASSOCIATED WITH ALTERED COPPER UPTAKE/TRANSPORT PATHWAYS IN THE AORTA OF STZ-DIABETIC RATS: EFFECTS OF TREATMENT BY CU(II)-SELECTIVE CHELATION

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Objectives: Cardiovascular disease is the commonest complication of diabetes. Previous studies from our group have identified diabetes-evoked changes in copper homeostasis that cause accumulation of chelatable-Cu(II) in the heart (1). We also showed that treatment by Cu(II)-selective chelation with TETA (triethylenetetramine) ameliorates cardiac left-ventricular/aortic damage in diabetes (2). This study aimed to define the pathogenic role of copper imbalance in diabetic arteriopathy and its response to TETA.
Methods: Pathological changes in the aorta of STZ-diabetic rats with/without TETA treatment were examined by histological and confocal imaging. Expression of genes and proteins involved in regulation of copper uptake/transport in aortic tissues were analysed by RT-qPCR and Western blotting.
Results: Diabetes-induced oxidative aortic damage was associated with increased expression of ET-1, ET-A, ICAM1 and eNOS, and decreased expression of Ctr1 (cell-membrane copper-uptake transporter-1) and Sco1 (copper-chaperone 1 for cytochrome c oxidase). We also identified up-regulation of CCS (copper chaperone for SOD1) and copper-binding metallothioneins (MT1/2) as further compensatory responses apparently aimed at up-regulating copper-related defences in response to altered aortic copper regulation in diabetes. TETA treatment further elevated MT1/2 levels. Moreover, diabetes lowered levels/activity of SOD2, both of which were restored by TETA treatment.
Conclusions: Dysregulation of cellular copper uptake/transport might be an important molecular process contributing to the pathogenesis of diabetic arteriopathy, and TETA treatment could be beneficial by restoring of these acquired defects, at least in part via activation of MT1/2 which are potent antioxidants, and SOD2, the main antioxidant enzyme that scavenges intra-mitochondrial superoxide radical.
References
(1) Cooper et al (2004) Diabetes. 53, 2501-2508.
(2) Gong et al (2006) Mol Pharmacol. 70, 2045-2051.

P4.28
GLYCAEMIC HOMEOSTASIS, ARTERIAL STIFFNESS AND DIASTOLIC FUNCTION IN HEALTHY SUBJECTS

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Objectives: To examine the impact of glycaemic homeostasis on arterial stiffness and cardiac diastolic function in healthy subjects.
Methods: Subjects (100 male & 115 female) were normotensive and normolipidaemic and had normal oral glucose tolerance test responses. Carotid-femoral arterial stiffness (PWV) and atherosclerotic risk (carotid intima media thickness; CIMT) were measured. Early/late mitral valve filling velocity (MV E/A) and isovolumetric relaxation time (IVRT) was used to assess diastolic function. Glycosylated haemoglobin (HbA_{1c}) was used to determine long-term glycaemic homeostasis. Anthropometrical measurements such as height, body mass and waist circumference were also measured.
Results: Spearman's correlation identified significant association between HbA_{1c} and age (r=0.40, P<0.0001), waist height ratio (r=0.18, P<0.01), PWV (r=0.26, P<0.001), CIMT (r=0.18, P<0.05), MV E/A (r=-0.37, P<0.0001) and IVRT (r=0.28, P<0.01). In multiple regression analysis's age remained the only independent predictor of PWV, CIMT, MV E/A and IVRT.
Conclusion: Despite being clinically healthy, HbA_{1c} is associated with greater arterial stiffness and poor diastolic function.

P4.29
COMPARATIVE EFFECTS OF ANTIHYPERTENSIVE DRUGS ON OXIDATIVE STRESS AND INFLAMMATION

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Objective: Oxidative stress and vascular inflammation are increased in hypertension. These factors may contribute to target organ damage and increased cardiovascular risk in these patients. We studied the effect of four classes of antihypertensive drugs on oxidative stress and inflammatory markers in patients with essential hypertension.
Design and method: In this double-blind placebo-controlled crossover study we randomized 41 treatment-naïve hypertensive patients to receive doxazosin 4 mg, candesartan 16 mg , bisoprolol 5 mg, isosorbide mononitrate 50 mg, and placebo daily for 6 weeks. Brachial blood pressure (BP), plasma high sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), asymmetric dimethylarginine (ADMA), oxidized LDL (oxLDL), soluble intercellular adhesion molecule-1 (sICAM-1), oxLDL antibodies (OLAB), and urine 8-isoprostanes were measured after each treatment period.
Results: All drugs reduced systolic, diastolic, and mean arterial pressure (p<0.001) with candesartan having the greatest effect. None of the drugs reduced inflammatory or oxidative stress markers compared to placebo. There were significant differences in between-drug analysis. Doxazosin reduced OLAB and oxLDL levels the most (p<0.05). With bisoprolol there was a trend for hsCRP and ADMA level increase compared to other drugs (p<0.01). There were no differences regarding drug effects on sICAM-1, IL-6, or 8-isoprostane levels. Changes in oxLDL and to lesser degree hsCRP and sICAM-1 levels correlated with change in BP with study drugs.
Conclusions: In our study an alpha-blocker seemed to have the most favorable effect on oxidative stress and inflammatory markers while a beta-blocker had least effect. These effects are partially dependent on the BP-lowering effects of the drugs.

P4.30
ENDOTHELIAL DYSFUNCTION AND CARDIOVASCULAR RISK PROFILE IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION

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Background/aims: The impact of chronic hepatitis C (HCV) virus infection on atherosclerosis is controversial. In this pilot clinical study, we examined whether HCV patients significantly differed in markers of subclinical atherosclerosis compared to patients with alcohol-related chronic liver disease.
Methods: We enrolled 21 consecutive adult patients with HCV and 11 patients with alcohol-related chronic liver disease after detoxification from alcohol. Common carotid intima-media thickness (CIMT) and brachial artery flow mediated vasodilation (FMD) by ultrasonography and carotid-femoral