A8491 CXCL1 3 and CCL18 genes are associated with essential hypertension in Tatars from Russia

Article *in* Journal of Hypertension · October 2018

DOI: 10.1097/01.hjh.0000548207.60119.27

4 authors, including:

Yanina Timasheva
Russian Academy of Sciences
52 PUBLICATIONS **94** CITATIONS

SEE PROFILE

Conclusion: 1 IMD can increase large particles and intermediate particles of HDL which have higher ApoA-I and PON-1 to exert anti-AS;2 IMD may elevate functional HDL by increasing LCAT activity.

Keywords: IMD atherosclerosis lipid metabolism HDL-C subtype

A8669 VASCULAR STIFFNESS IN TRUE RESISTANT HYPERTENSIVE PATIENTS AFTER RENAL DENERVATION: DOES PLASMA ALDOSTERONE MATTER?

Mikhail Ionov, Natalia Avdonina, Svetlana Mironova, Igor Emelyanov, Dmitry Zverev, Nadezhda Zvartau, Alexandra Konradi. *Cardiology V.A. Almazov NMRC Russia*

Objectives: Resistant hypertension (RHTN) is characterized by higher vascular damage by excess in arterial stiffness assessed by pulse wave velocity (PWV) and renal resistive index (RRI). RHTN is associated with increased renin-angiotensin-aldosterone system (RAAS) activity promoting vascular fibrosis. Aim of the study was to evaluate the link between vascular damage and plasma aldosterone concentration (PAC) in RHTN patients before and after renal denervation (RD).

Methods: Consequent 25 patients (mean age 56 ± 10 years, 9 males) with confirmed true RHTN with standardized multidrug combination treatment underwent RD (Symplicity RDN System, Medtronic, USA). Markers of vascular damage, office blood pressure (BP) and PAC were evaluated before and twelve months after procedure. RRI was noninvasively assessed by ultrasonography (Vivid 7 Dimension, GE, USA), PWV was calculated by applanation tonometry (SphygmoCor XCEL, AtCor Medical, Australia). Aldosterone plasma concentration (reference values 10–105 pg/ml) were determined by immunofluorescence method.

Results: SBP and DBP dropped (−24.5/−13.2 mmHg, respectively; $p < 0.05$) a year after RDN. Arterial stiffness (PWV) improved 12 months after procedure (10.1 ± 1.8 to 9.3 ± 2.0 m/s, $p < 0.05$). RHTN patients characterized by rather high RRI at baseline and values remained unchanged during follow-up (0,7 ± 0,08 and 0,71 ± 0,08 respectively; $p = 0,87$). PAC slightly but significantly decreased a year after procedure (−13.6 ± 6 pg/ml, $P = 0.008$). Delta PWV was associated both with decrease of PAC ($r = 0.562$, $p = 0,04$) and BP levels ($r = 0.546$, $p = 0.03$) with no association between RRI, PAC and BP.

Conclusion: Effective treatment of RHTN improves vascular stiffness partly through decrease of BP and aldosterone levels. However no change in renal RRI detected without clear link to BP or RAAS activity.

Keywords: hypertension, renal denervation, vascular stiffness, aldosterone, RAAS

A8491 CXCL1 3 AND CCL18 GENES ARE ASSOCIATED WITH ESSENTIAL HYPERTENSION IN TATARS FROM RUSSIA

Yanina Timasheva[1], Timur R Nasibullin[2], Alara N Zakirova[3], Olga E Mustafina[2], Yanina Timasheva[4]. [1]*Genomics Institute of Biochemistry and Genetics UFRC RAS Russia,* [2]*Department of Physiological Genetics Institute of Biochemistry and Genetics UFRC RAS Russia,* [3]*Department of Cardiology Bashkir State Medical University Russia,* [4]*Department of Medical Genetics and Fundamental Medicine Bashkir State Medical University Russia*

Objectives: Our aim was to evaluate the role of inflammation-related genes in essential hypertension (EH) and blood pressure (BP) control.

Methods: We analysed transcriptional activity of inflammatory mediator genes in EH patients and normotensive individuals using real-time PCR primer assays (SABiosciences, Qiagen, USA), and genotyped polymorphisms in 20 differentially expressed genes (IL10, IL1B, CXCR4, CXCR2, CCR5, CCR2, CX3CR1, CXCL1, CXCL8, IL12B, LTA, TNF, IL6, TNFRSF1A, CCL17, CCL2, CCL8, CCL16, CCL23, and CCL18) in the study group consisting of 737 men (274 patients with EH and 463 controls) of Tatar ethnic origin from the Republic of Bashkortostan (Russian Federation). We analysed association with EH and BP levels using logistic and linear regression models implemented in PLINK with age as covariate. Multilocus analysis was performed using APSampler program. FDR method was applied to adjust for multiple testing.

Results: The most significant associations with EH were observed for CXCL13 rs355689*C allele (OR = 0.55, CI: 0.39–0.76, PFDR = 0.008, additive model) and CCL18 rs8073066*C allele (OR = 0.64, CI: 0.49–0.83, PFDR = 0.018, additive model). CXCL13 rs355689*C allele was associated with systolic (PFDR = 0.002, additive model) and diastolic (PFDR = 0.025, dominant model) BP levels. Multilocus analysis has revealed additional association of IL1B rs16944*T+ CXCL1 rs40748G +TNFRSF1A rs767455*G+ CCL2 rs991804*C (OR = 2.9, PFDR = 0.01) and CX3CR1 rs3732378*T+ CXCL13 rs355689*C + CCL17 rs223828*T (OR = 0.22, PFDR = 0.001) combinations with EH.

Conclusion: Using expression profiling, we detected differential transcriptional activity of 20 inflammation-related genes in EH patients, and found the association of the two of them (CXCL13 and CCL18) with the EH risk. Our findings suggest the implication of chemokines in hypertension.

Keywords: essential hypertension, inflammation, chemokines

A9953 TELMISARTAN INHIBITS THE AUTOCRINE ROLE OF LEPTIN IN MEDIATING CARDIOMYOCYTE REMODELING IN HYPERTENSIVE LEFT VENTRICULAR HYPERTROPHY RATS THROUGH THE ANGIOTENSIN II–ANGIOTENSIN II TYPE I RECEPTORS AND PEROXIDASE PROLIFERATOR-ACTIVATED RECEPTORS-γ PATHWAYS

Min Li[1], Lei Liu [2], Gang Tian[2]. [1]*Xi'an Jiaotong University First Affiliated Hospital China, People's Republic of,* [2]*Xi'an Jiaotong University First Affiliated Hospita China, People's Republic of*

Objectives: To confirm myocardium autocrine leptin production is involved in stress-overload hypertensive left ventricular hypertrophy, and telmisartan may alleviate myocardial fibrosis and reverse hypertensive left ventricular hypertrophy by inhibiting leptin autocrine function.

Methods: Eight-week male Sprague–Dawley (SD) rats (weight:180–230 g) were used to establish the left ventricular hypertrophy model through abdominal aortic constriction.

Results: The expression of AngII–AT1R in the myocardial tissue of pressure-overload hypertensive left ventricular hypertrophy rats increased. AngII promotes the nuclear translocation of intracellular activation protein 1 and the synthesis of leptin, as well as leptin release from myocardial tissue through the AT1R–ROS–ERK1/2 pathway. AngII also participates in the imbalance in matrix metalloproteinase (MMP)–tissue inhibitor of metalloproteinase (TIMP) and in the dynamic balance of myocardial extracellular matrix (ECM) collagen synthesis and degradation. The leptin produced by the myocardial-tissue-induced changes in myocardial TGF-β1/Smad3 and JAK2/STAT3 signaling pathways during stress-overload hypertensive left ventricular hypertrophy promotes myocardial fibrosis through the leptin receptor. Long-term telmisartan treatment reduces myocardial leptin autocrine function by inhibiting the AT1R–ROS–ERK1/2 pathway, as well as restores the MMP/TIMP balance and reverses myocardial fibrosis by stimulating PPAR-γ to inhibit the JAK2/STAT3–TGF-β1/Smad3 signaling pathway.

Conclusion: Hypertensive left ventricular hypertrophy is closely related to the autocrine function of leptin, which is a adipokine in myocardium. A new mechanism for reversing hypertensive left ventricular hypertrophy was discovered and is shown to involve ARB telmisartan with PPAR-γ activation.

Keywords: Left Ventricular Hypertrophy, Cardiomyocyte Remodeling, Autocrine, Leptin, Telmisartan

A9052 EFFECT OF RENAL DENERVATION ON HYPOTHALAMUS P38MAPK AND P65NFKB SIGNAL PATHWAY IN SHR RATS

Xu Mengping[1], Chengzhi Lu[2]. [1]*Cardiovascular Department Tianjin First Center Hospital China, People's Republic of,* [2]*Cardiovascular Department Tianjin First Center Hospital, China China, People's Republic of*

Objectives: This study is to observe the change of hypothalamic AngII, AT1R, p38MAPK and p65NFκB before and after renal denervation on spontaneously hypertensive rats, to observe the effect of renal denervation on MAPK and NFKB signaling pathway.

Methods: 36 SHR rats were divided into three groups randomly: SHR blank group, RDN group and sham group. Choose the same age WKY rats as the blank control group (WKY group, n = 12). The SHR RDN group and sham group were given RDN or sham operation, then were killed respectively 1 week and 6 week after RDN (D1 group, n = 6; D6 group, n = 6), as well as 1 week and 6 weeks after sham operation (S1 group, n = 6; S6 group, n = 6). Kidney and hypothalamus were collected for examination. The content of plasma S100B, NSE, kidney NE and hypothalamic AngII were determined by ELISA. The protein expression of p38MAPK, p-p38MAPK and p65NFkB in hypothalamus were determined by Westerm-Blot. The mRNA expression of AT1R and P38MAPK in hypothalamus were detected by real-time PCR.

Results: In SHR blank group, the level of blood pressure, the content of hypothalamic AngII, kidney NE, plasma NSE, S100B and the expression of AT1R, p38MAPK, p-p38MAPK and p65NFkB increased significantly compared with WKY group ($p < 0.05$). The blood pressure in D1 group decreased significantly compared with the S1 group ($p < 0.05$). The blood pressure in D6 group

Conclusion: Renal denervation can significantly decrease the level of NE in kidney and effectively lower blood pressure of SHR rats in a short term. By