T. Sakurada; K. Miyako; Y. Horinouchi; K. Teraoka; T. Kujime; K. Kawazoe; H. Houchi; T. Tamaki; and K. Minakuchi

Introduction: Oxidative stress and endothelial damage are involved in the development and progression of diabetic nephropathy (DN). In this study, we investigated the effects of nitrosonifedipine (NO-NIF) having antioxidative property on DN with the endothelial dysfunction.

Patients (or Materials) and Methods: KKAy mice were used as a model of developing type II diabetes mellitus with the endothelial dysfunction. NO-NIF (30 mg/kg/d) was administrated continuously by intraperitoneal injection for 4 weeks. Histologic changes in the kidney, urinary protein, urinary albumin, oxidative stress, and blood glucose levels were evaluated. Moreover, we also examined whether NO-NIF affected the kidney dysfunction in eNOS knockout mice.

Results: In NO-NIF–treated KKAy mice, the urinary protein and albumin were significantly decreased compared with nontreated KKAy mice. The pathologic analysis showed expanded glomerular mesangium in KKAy mice, which was suppressed by NO-NIF administration. However, NO-NIF had no effect on blood glucose in KKAy mice. NO-NIF decreased dihydroethidium staining in the kidney and 8-hydroxy-2-deoxyguanosine in the urine in KKAy mice. The expression of intercellular adhesion molecule-1, an endothelial cell damage marker, was decreased in the kidney by NO-NIF while the podocyte injury marker was not changed. The mRNA expression of TNF-α in kidney was also inhibited by NO-NIF. Furthermore, the administration of NO-NIF also suppressed the expansion of glomerular mesangial area and decreased urinary albumin in eNOS knockout mice.

Conclusion: NO-NIF prevents renal dysfunction associated with endothelial dysfunction independently of the blood glucose lowering, and it might be a potential drug for the prevention of DN.

Disclosure of Interest: None declared.
Clinical Therapeutics

PP092—CHANGES IN VASCULAR REACTIVITY CAUSED BY ANGIOTENSIN II IN ISOLATED VESSELS OF RAT AORTA IN A MODEL OF HYPERTENSION
E.M. Lopez-Calderon1; L.N. Acevedo-Villavicencio1; G.C. Villanueva-Lopez1; E. Lara-Padilla1; G. Guevara-Balcasar1; E. Hong-Chong2; and M.C. Castillo-Hernandez3

1Seccion de estudios de Posgrado e Investigacion, Escuela Superior de Medicina del Instituto Politecnico Nacional; and
2Farmacobiologia, Centro de Investigacion y Estudios Avanzados, sede Sin, Mexico City, Mexico

Introduction: Hypertension (HBP) is a disease with high morbidity and mortality worldwide and is a major etiological factor in heart and vascular diseases. An important regulatory mechanism of blood pressure (BP) is the renin angiotensin system (RAS). In fact, all the first-line drugs for the treatment of hypertension act on some component of the RAS. However, these treatments frequently lead to the development of changes in morphology and physiology characterized by vascular complications. It is therefore necessary to consider adjuvant therapies to improve the outcome of treatments and therefore in the quality of life of patients with HBP. A therapy that has been shown to improve the clinical condition of patients with HBP is hyperbaric oxygenation (HBO), in which the patient is subject to a pressure of 2 atmospheres absolute with an oxygen concentration of 100%. This therapy has been shown to improve vascular smooth muscle relaxation, although the mechanism of action has not yet been specified. The aim of this study is to examine the role of the RAS in the relaxation of vessels in hypertensive rats that is produced by HBO.

Patients (or Materials) and Methods: Male Wistar rats were used (340 ± 20 g) at standard conditions (light/dark cycle, water and food ad libitum), and hypertension was induced by a previously described surgical method (PAGE). Stable hypertension was established at 7 days’ postsurgery (for plethysmographic method). On the eighth day, HBO therapy began, and was carried out 5 days per week for 4 weeks. Rats were sacrificed at the end of treatment, obtaining thoracic and abdominal aorta. The endothelium was removed by a mechanical method, aortic rings were mounted, and concentration response curves were constructed according to increasing doses of ANG II for all groups with and without HBO. The results are analyzed with 2-way ANOVA and post hoc Von Ferroni.

Results: Diastolic pressure was found to be 150 (10) mm Hg, consistent with the definition of hypertension. The angiotensin contractile response was lower in the groups of rats treated with HBO, compared with the 2 control groups (untreated and SHAM animals).

Conclusion: HBO therapy reduced vascular reactivity in both segments of the hypertensive rat aorta. This suggests that HBO could possibly be used with hypertensive patients to reduce the use of drugs in therapy.

Disclosure of Interest: None declared.

PP094—TARGETS OF THERAPY OF PATIENTS WITH CONGESTIVE HEART FAILURE CAUSED BY ISCHEMIC HEART DISEASE AND DIABETES
Ll. Megreladze1; N.V. Gogadze1; T.D. Kezeli2; K.S. Kakabadze1; M.G. Mirzashvili1; Z.V. Chapachadze1; and G.V. Sukoyan3

1Tbilisi State Medical University; 2Javakhishvili State Medical University; 3Drug Agency; and 4Biotechpharm GE, Tbilisi, Georgia

Introduction: Congestive heart failure (CHF), caused by ischemic cardiomyopathy and diabetes II-type, is a devastating clinical problem. The aim of this study was to highlight several advances in the understanding of molecular pathways involved in cardiac hypertrophy, inflammatory signaling, and oxidant stress that may play a key role in altering transcriptional regulatory networks regulating adaptation or maladaptation, and consequently, the transition to overt HF.

Patients (or Materials) and Methods: A total of 56 patients aged 53 (6) years, with ischemic cardiomyopathies (ICMP) accompanied by diabetes II-type were included in the study. Entry criteria were: the left ventricular ejection fraction (LVEF) < 40% and mild LV dilatation, symptoms of CHF for the last 2 months, at least. All patients included in the study were randomized into 2 groups; control received standard therapy (digoxin 0.25 mg per day, inhibitor of ACE and a diuretic, n = 29) and the main one (n = 30) an inhibitor of ACE, a diuretic, and Adenocin (2 ampoules diluted in 50-100 mL of saline in infused IV). There were no significant differences in baseline characteristics (demographic and anamnesis) between groups. Plasma levels of cytokines (interleukine-1 [IL-1], tumor necrosis factor [TNF-α], redox-potential NAD/NADH, superoxide anion production, activities of superoxide dismutase (SOD), and catalase (CT) were determined.

Results: It has been shown that in the control group, the functional class (FC) of CHF by NYHA decreased by 12%, the dyspnea by 49%, lung congestion by 78%, hepatomegaly by 70%, and peripheral edema improved by 45%. The total CHF score improved by 52%. In the main group, the FC of CHF improved by 25%, dyspnea and lung congestion disappeared completely, hepatomegaly improved by 74%, peripheral edema -by 88%. The total score improved by 67%. In the group receiving Adenocin, LVEF improved by 16% (from 26% to 42%), stroke volume improved by 28%. Hence, the optimal treatment of CHF would be achieved through increase in the energy supply: redox-potential NAD/NADH increased by 34%, the content of pyridine nucleotide in the plasma by 40%. The activity of the marker of hyperactivation of the system of reactive oxygen production decreased by 48% and activities of SOD and CT increased by 45% and 60%, respectively. Treatment with Adenocin leads to a markedly improve of the state of immune system and as a result the content of proinflammatory cytokines, IL-1β and TNF-α decreased by 49 and 38%, respectively.

Conclusion: The modern approach to treatment of HF is multidisciplinary, given that mandatory multorgan attention is required to ensure early good outcome in these high-risk patients with ICMP and diabetes II-type. From the present results, it is evident that Adenocin cessates cardiac remodeling during the development of cardiac hypertrophy and resores functional activity of the myocardium.

Disclosure of Interest: None declared.