EFFECTS OF APOCYNIN TREATMENT AND HBO PRECONDITIONING ON IMMUNOHISTOCHEMICAL 4-HNE, HIF1 ALPHA, HIF2 ALPHA AND NGAL TISSUE EXPRESSION IN POSTISCEMIC ACUTE KIDNEY INJURY IN SHR RATS

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Objective: Oxidative stress has been considered as a central aggravating factor in the development of postischemic acute kidney injury (AKI). 4-hydroxynonenal (4-HNE) is a product of lipid peroxidation and may serve as non-invasive biomarker of oxidative stress while neutrophil gelatinase-associated lipocalin (NGAL) is a biomarker of AKI. Hypoxia-inducible factors (HIFs) are the "master" transcription factors responsible for gene expression in hypoxia, which play an important role in kidney injury and repair by regulating HIF target genes, including microRNAs.

Design and method: The study was conducted on male SHR rats, randomly divided into following groups: sham-operated group (SHAM) AKI control group, AKI group with apocynin treatment (AKI+APO), group with HBO preconditioning before AKI induction (AKI+HBO) and group with HBO preconditioning before and apocynin treatment after AKI induction (AKI+APO+HBO). HBO preconditioning was performed by exposing to pure oxygen (2.026 bar) twice a day for two consecutive days for 60 minutes, and 24 h before AKI induction. Apocynin, NADPH oxidase inhibitor was injected 5 minutes before reperfusion.

Results: AKI induction significantly decreased creatinine (CCr), urea (CU) and phosphate (CPhos) clearances when compared to SHAM group. Remarkable increase in CCr, CU, CPhos levels were observed in all treated groups (AKI+APO, AKI+HBO, AKI+APO+HBO) in comparison to AKI group. Sham – operated rats did not express 4-HNE and NGAL in any parenchymal structure. AKI induced abundant and strong glomerular expression of 4-HNE along with expression in interstitial compartment. All treatments (AKI+APO, AKI+HBO, AKI+APO+HBO) significantly decreased 4-HNE expression both in glomeruli and interstitium. Also, AKI stimulated widespread NGAL expression in renal epithelial tubular cells with fine granular appearance on the apical surface of the cells, affecting entire circumference of tubular cross-sectioning, which was decreased in all treated groups. In SHAM group, the expression of HIF1 alpha and HIF2 alpha was focal with weak intensity in glomeruli and interstitium. In AKI group, the expression was diffuse and strong, with remarkable improvement in all treated groups.

Conclusions: Considering our results, we can conclude that apocynin treatment, as well as HBO preconditioning may have protective effects in postischemic acute kidney injury induced in spontaneously hypertensive rats.

TRAJECTORIES OF BLOOD PRESSURE, TREATMENT PATTERNS AND HYPERTENSION CONTROL IN PATIENTS WITH LUPUS NEPHRITIS – DATA FROM A RETROSPECTIVE COHORT STUDY

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Objective: Prevalence of hypertension seems to be higher in patients with systemic lupus erythematosus (SLE) than in the general population, but there is scarce data on the epidemiology of hypertension in lupus nephritis (LN). Furthermore, to the best of our knowledge, there are no studies examining the trajectories of blood pressure (BP), treatment patterns and control of hypertension in LN.

Design and method: We have conducted a retrospective cohort study to evaluate the prevalence, treatment and control of hypertension in patients with biopsy-proven LN. We have collected data on demographics, clinical and laboratory parameters, histopathology and office BP measurement at the time of biopsy and after long-term follow-up. BP measurement and definition of hypertension were according to 2018 ESC/ESH guidelines.

Results: A total of 36 patients with biopsy-proven LN were followed up for 4.5 ± 2.9 years (81% women, mean age at biopsy 38 ± 14). Mean duration of SLE prior to biopsy was 4.3 years (min-max 0 to 27 years). Both systolic and diastolic BP decreased from the time of biopsy to last follow-up (137/85 mmHg vs. 125/79 mmHg, $p < 0.001$ for systolic BP and $p = 0.075$ for diastolic BP). Prevalence of hypertension at the time of biopsy was 58% and increased to 72% at the time of last follow-up ($p = 0.22$). Mean number of drugs per patient did not change (2.0 vs. 1.8, $p > 0.05$). Only 48% and 58% of patients with hypertension had achieved BP control ($p = 0.67$) and a total of 1 and 2 patients had resistant hypertension at the time of biopsy and at last follow-up, respectively. When examining treatment, 67% and 77% patients with hypertension had an ACEI/ARB, while 48% and 38% had calcium channel blocker, 43% and 35% had diuretics and 24% and 31% had beta blockers at the time of biopsy and follow-up, respectively.

Conclusions: LN is associated with high cardiovascular risk and mortality as well as a high prevalence and inadequate control of hypertension. Achieving BP control is crucial and should be an important therapeutic goal in these patients.

RENAL MICROPERFUSION RESPONSE TO A COLD PRESSURE TEST IS DECREASED IN HYPERTENSIVE PATIENTS

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Objective: Microcirculation is essential to supply oxygen and nutriments to tissue. Alteration in the microcirculation is often proposed as a mechanistic link between hypertension and target organ damage. The recent developments in contrast-enhanced ultrasonography (CEUS) have enable the quantification of renal microcirculation. The objective of this study was to compare the microcirculatory response during a cold pressure test (CPT) in hypertensive (HT) patients with those in healthy normotensive (NT) participants.

Design and method: This was a prospective case-control study. Hypertensive (HT) and normotensive (NT) participants underwent two separate CPT of 2 minutes. Doppler ultrasound was used to measure renal resistive index (RRI) and CEUS to measure the perfusion index (PI) as a proxy of renal tissue microcirculation. Renal Doppler and CEUS were performed before and during the CPT. We compared baseline measures and responses to CPT of HT and NT groups using a Wilcoxon test.

Results: Sixteen hypertensive and nineteen normotensive male participants were included. HT participants were older and had higher blood pressure and body mass index. Baseline RRI was similar in both group, but HT had lower PI (median with interquartile range): 1083 U(447–1476) vs 1772 U(1295–2557), $p = 0.016$. The CPT decreased the RRI in NT and increased the RRI in HT, resulting in a different CPT response -0.026 [CI -0.045; -0.008, $p = 0.006$]. The CPT increased the PI in both groups but the response was blunted in HT patients - 755U ± 518, ($p = 0.01$).

Conclusions: Compared to healthy participants, hypertensive patients show a paradoxal RRI response and a lower increase in perfusion index during CPT suggesting that microcirculation and possibly renal autoregulation is altered. This is the first demonstration showing that CEUS enables the detection of microcirculatory differences between healthy participants and hypertensive patients.

UPREGULATION OF NADH/NADPH OXIDASE 4 BY ANGIOTENSIN II INDUCES PODOCYTE APOPTOSIS

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Objective: Angiotensin II induces glomerular and podocyte injury via systemic and local vasoconstrictive or non-hemodynamic effects including oxidative stress. The release of free radicals from podocytes may participate in the development of glomerular injury and proteinuria. We studied the pathophysiologic roles of oxidative stress in angiotensin II-induced podocyte apoptosis.

Design and method: Mouse podocytes were incubated in media containing various concentrations of angiotensin II and at different incubation times and transfected by Nox4 or AT1R siRNAs or negative control scrambled siRNA for 24 h. The changes of podocyte oxidative stress and apoptosis were observed by confocal imaging, western blotting, realtime PCR, FACS and TUNEL assay according to the presence of angiotensin II.

Results: Angiotensin II increased the generation of mitochondrial superoxide anions and reactive oxygen species levels but suppressed superoxide dismutase activity that was reversed by probucol, an antioxidant. Angiotensin II also in-