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ABSTRACT BOOK

$p < 0.01$), p22phox of NAD(P)H oxidase, (100±13.6 *vs.* 186±20; $p < 0.05$) and SOD (100±5.6 *vs.* 159±20; $p < 0.05$) was higher than in SO-rats. In contrast, aortic mRNA expression of XD, catalase, VEGF and TGF-β were comparable in both groups. Serum levels of IL-6 and IL-1β were higher in PPH-rats (109±6.6 and 64.5±2.7 respectively, $p < 0.05$) that SO-rats (57.7±11.6 and 49.3±4.5 respectively) and IL-10 was comparable in both groups.

Conclusion: Experimental PPH in rats is associated with increased aortic expression of fibrotic, oxidative and inflammatory factors, suggesting that this hemodynamic hepatic alteration could lead to the development of distal vascular damage.

P29.394 VASCULAR FUNCTION MODIFICATION IN THE MODEL OF LONG-TERM CONTINUOUS LIGHT-INDUCED HYPERTENSION OF RATS

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Objective: Exposure of rats to continuous light results in hypertension development. There is shortage of data on peripheral blood vessels function in this particular model of hypertension. We investigated whether 6-week exposure of Wistar rats to continuous 24h/day light can deteriorate vascular function with the focus on potential protection by vasoactive drugs.

Method: Experiments were performed on male adult normotensive Wistar rats divided into five groups: (a) control Wistar rats − exposed to normal light/dark cycle (12h/day light, 12h/day dark); (b) rats exposed to continuous light (24h/day); (c) control rats + N^G-nitro-L-arginine methyl ester (L-NAME); (d) Wistar rats exposed to continuous light + L-NAME; (e) Wistar rats exposed to continuous light + L-NAME + captopril. Blood pressure was measured weekly by tail-cuff technique. Rings of isolated thoracic aortas were suspended in organ baths containing modified Krebs solution and connected to a force-displacement transducer for the recording of isometric tension.

Results: The prolonged exposure of Wistar rats to continuous light for 6 weeks, beginning at 12 weeks of age, induced elevation of blood pressure from 124±1 mmHg (controls) to 151±1 mmHg. In controls, L-NAME treatment increased blood pressure to 173±1 mmHg, and in rats with continuous light even to 183±1 mmHg. Simultaneous treatment with angiotensin-converting enzyme inhibitor, captopril, normalized blood pressure despite continuous light exposure. Continuous light application induced deterioration of endothelium-dependent relaxation in isolated rings of the thoracic aorta. Also L-NAME administration alone or in combination with continuous light decreased endothelium-dependent relaxation. This inhibitory effect was partially reversed by the simultaneous captopril administration. Moreover, continuous light exposure, as well as L-NAME treatment or their concomitant action, increased sensitivity of aortic smooth muscle to exogenous noradrenaline.

Conclusions: The results indicate that long lasting exposure of Wistar rats to continuous light results in elevation of blood pressure and modification of vascular responses to vasoactive drugs. This effect could be, at least in part, mediated by diminution of nitric oxide production.

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P29.395 PIOGLITAZONE ALTERS THE PARTICIPATION OF CYCLOOXYGENASE-2 PRODUCTS AND REACTIVE OXYGEN SPECIES ON VASCULAR REACTIVITY IN HYPERTENSIVE RATS

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The nuclear receptor peroxisome proliferator-activated receptor-γ (PPARγ) is expressed in all major vascular cells, where it may play an important role in vascular diseases. Thus, the PPARγ agonists, glitazones, exert depressor action in both hypertensive subjects and various animal models, improve endothelium-dependent vasodilation, and reduce vascular contractility in response to different vasoconstrictors. In addition, glitazones have anti-inflammatory actions associated to interference with redox-sensitive transcription factors, such as NF-κB, involved in the transcription of several genes including COX-2.

Objective: To analyze the effect of chronic pioglitazone treatment on the vascular reactivity of mesenteric resistance arteries from spontaneously hypertensive rats (SHR) to phenylephrine, as well as the role of prostanoids and reactive oxygen species in such effect.

Methods: Mesenteric resistance arteries from 6- month old SHR rats untreated or treated with the PPARγ activator pioglitazone (2.5 mg/kg/day for 28 days) were used. Vascular reactivity was studied with wire myography and protein expression by western blot.

Results: Pioglitazone did not lower blood pressure of SHR (control: 198.9±3.3; pioglitazone: 200±5.2 mmHg; $P > 0.05$). Concentration-response curve to phenylephrine (0.1−30 μM) was similar in segments from untreated and pioglitazone-treated rats. Indomethacin (10 μM), the selective COX-2 inhibitor NS 398 (1 μM), the TxA_2 receptor antagonist SQ 29,548 (1 μM) and the EP_1 receptor antagonist SC 19220 (10 μM) reduced the response to phenylephrine only in segments from treated rats, while the TxA_2 synthase inhibitor furegrelate (1 μM) did not modify this response in both treated and untreated rats. In addition, COX-2 expression was higher in mesenteric arteries from treated than untreated rats. Pioglitazone treatment abolished the inhibitory effect of the respective inhibitors of NADPH oxidase and xanthine oxidase, apocynin (0.3 mM) and allopurinol (0.3 mM) on vasoconstrictor responses to phenylephrine.

Conclusions: Chronic pioglitazone treatment of hypertensive rats increases mesenteric COX-2 expression, associated with increased participation of contractile prostanoids from COX-2 in vasoconstrictor responses to phenylephrine. On the other hand, the observed reduction of involvement of NADPH oxidase and xantine oxidase-derived reactive oxygen species in the contraction elicited by phenylephrine can explain the similar vasoconstrictor response to this agonist found in resistance arteries. If pioglitazone regulates reactive oxygen species production needs to be elucidated.

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P29.396 BETA-ADRENERGIC VASODILATION OF ISOPRENALINE IS LARGELY PREVENTED BY ENDOGENOUS NITRIC OXIDE IN CONSCIOUS WISTAR BUT NOT IN SHR RATS

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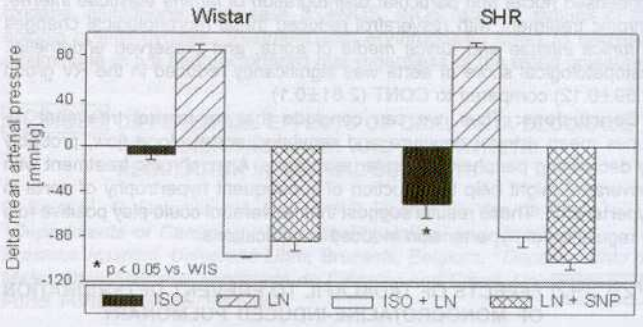
Objective: High blood pressure (BP) in spontaneously hypertensive rats (SHR) is generally attributed to the increased activity of sympathetic nervous system (SNS) and/or impaired vasodilator action of endothelial-derived NO system. Our previous studies have shown no differences in the dose-response curves to norepinephrine in conscious normotensive Wistar (WIS) and SHR. Thus, high dependence of BP on SNS in SHR could result from excessive catecholamine release from nerve endings and/or the imbalance between vasoconstrictive alpha-adrenoceptor and vasodilator beta-adrenoceptor action. We focused our attention on the contribution of NO-dependent or beta-adrenergic vasodilation to BP regulation in WIS and SHR rats.

Design and Methods: The effect of beta-adrenoceptor stimulation was determined using continuous infusion of isoprenaline (ISO, 100 ng/kg/min i.v.) with or without previous inhibition of NO formation by L-NAME (LN, 30 mg/kg i.v.). The effect of NO donor sodium nitroprusside (SNP, 20 ug/kg i.v.) was studied under the conditions of acute NO deficiency.



Results: Isoprenaline infusion without previous inhibition of NO formation by L-NAME decreased BP more in SHR than in WIS rats. Following acute inhibition of NO formation, which caused the same BP increase in both rat strains, this L-NAME effect was completely abolished by subsequent isoprenaline infusion in both WIS and SHR (isoprenaline effects being completely reversed by beta-adrenoceptor blockade with propranolol, 1 mg/kg i.v.). Exogenous NO (delivered by SNP injection under the conditions of acute