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P173: COUPLED NITROSO-SULFIDE SIGNALIZATION TRIGGERS SPECIFIC VASOACTIVE EFFECTS IN INTRARENAL ARTERIES OF PATIENTS WITH ARTERIAL HYPERTENSION

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VOLUNTARY LIQUORICE INGESTION INCREASES BLOOD PRESSURE VIA MULTIPLE MECHANISMS: INCREASED VOLUME LOAD, PERIPHERAL ARTERIAL RESISTANCE, AND DECREASED AORTIC COMPLIANCE

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Objectives: Liquorice consumption elevates blood pressure [1-3], but the liquorice-induced haemodynamic changes in the upright position are unknown. We investigated haemodynamics after liquorice exposure in healthy volunteers during orthostatic challenge.

Methods: Haemodynamics were recorded from 22 normotensive subjects during passive 10- minute head-up tilt before and after two weeks of liquorice consumption (glycyrrhizin dose 290—370 mg/day) using radial pulse wave analysis, whole-body impedance cardiography, and spectral analysis of heart rate variability. Thirty age-matched healthy subjects maintaining their habitual diet served as controls.

Results: Liquorice ingestion elevated radial systolic (p < 0.001) and diastolic (p = 0.018) blood pressure and systemic vascular resistance (p = 0.037). During orthostatic challenge, heart rate increased less after the liquorice versus control diet (p = 0.003) and low frequency power of heart rate variability decreased within the liquorice group (p = 0.034). Liquorice intake increased central pulse pressure (p < 0.001) and augmentation index (p = 0.002) supine and upright, but in the upright position the elevation of augmentation index was accentuated (p = 0.007). Liquorice diet also increased extracellular fluid volume (p = 0.024) and aortic to popliteal pulse wave velocity (p = 0.027), and aortic characteristic impedance in the upright position (p = 0.002).

Conclusions: In addition to increased extracellular fluid volume and large arterial stiffness, two weeks of liquorice ingestion elevated systemic vascular resistance and augmentation index. Measurements performed at rest may underestimate the haemodynamic effects of liquorice ingestion, as enhanced central wave reflection and reduced chronotropic response were especially observed in the upright position.

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COUPLED NITROSO-SULFIDE SIGNALIZATION TRIGGERS SPECIFIC VASOACTIVE EFFECTS IN INTRARENAL ARTERIES OF PATIENTS WITH ARTERIAL HYPERTENSION

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In normotensive conditions, it has been confirmed that S-nitrosothiols, as a source of NO, interact with hydrogen sulfide (H_2S) and create new

substance/s with specific vasoactive effects. This interaction could represent new regulator pathway also in hypertension. The aim of the study was to investigate the vasoactive effects of H_2S , GSNO, and products of H_2S /GSNO interaction in lobar arteries isolated from kidney after nephrectomy of patients suffering from arterial hypertension.

Changes in isometric tension after pre-contraction were evaluated. Acetylcholine- induced vasorelaxation was significantly reduced compared to the effect induced by exogenous NO donor, sodium nitroprusside, probably suggesting an endothelium dysfunction. While 1 μ mol/l Na2S had a minimal effect on the vascular tone, 20 μ mol/l evoked a slight vasorelaxation. GSNO at 0.1 μ mol/l induced vasorelaxation which was significantly smaller compared to the effect induced by 1 μ mol/l. The mixture of GSNO (0.1 μ mol/l) and Na2S (1 μ mol/l) induced significantly higher vasorelaxation compared to GSNO (0.1 μ mol/l) alone only in 5th minute without the differences in the speed. On the other hand, the mixture prepared from higher concentrations of GSNO (1 μ mol/l) and Na2S (10 μ mol/l) induced a significantly higher (in 1st, 2nd, 5th, 10th minute) and faster vasorelaxation compared to the effect induced by GSNO (1 μ mol/l) alone.

In conditions of arterial hypertension $\rm H_2S$ in interaction with GSNO regulated a vasoconstrictor-increased arterial tone towards of more pronounced vasorelaxation compared to GSNO alone. We confirmed for the first time that specific vasoactive effects of coupled nitroso-sulfide signalization were triggered also in human arterial tissue.

References

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HEMODYNAMIC AND AUTONOMIC EFFECTS OF LOW-DOSE GLYCERYL TRINITRATE USED TO TEST ENDOTHELIUM-INDEPENDENT VASODILATION OF THE BRACHIAL ARTERY

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Background/Aim: Smooth muscle function is explored by sublingual glyceryl trinitrate (GTN) administration in vascular function protocols, in order to compare with endothelium- dependent vasodilation of the brachial artery by flow-mediated dilation (FMD). The aim of this study is to evaluate the hemodynamic and autonomic effects of the two most often used GTN dosages

Methods: In 80 essential hypertensive patients (HT) and 60 normotensive subjects (NT), we evaluated FMD of the brachial artery and endothelium-independent response to 25 and 400 mg of sublingual GTN by high-resolution ultrasound and automated image analysis. In a subgroup of 10 HT, muscle sympathetic nerve activity (MSNA) was also assessed by microneurography. **Results:** NT showed significantly (p < 0.01) lower FMD (5.5 \pm 3.3%) as compared to healthy controls (6.9 \pm 2.2%). The response to GTN 25 μg also tended to be lower (HT $7.2 \pm 3.3\%$; NT $7.9 \pm 2.9\%$; p = 0.06), whereas response to GTN 400 μg was similar (HT 14.3 \pm 4.8%, NT 14.5 \pm 54.7%, p = ns). In the whole population, changes in blood pressure (BP) induced by GTN 400 μg (systolic BP -3.2 ± 7.7 , diastolic BP $-4.7\pm5.0\,\mathrm{mmHg}$) were significantly higher (<0.001) compared to GTN $25\mu g$ (systolic BP -0.7 ± 5.8 , diastolic BP -0.7 ± 4.4 mmHg). Changes in heart rate were also higher with GTN 400µg than with 25µg (+5.6 $\pm\,6.4$ versus -0.2 ± 5.4 bpm, p < 0.001). This behavior was similar in HT and NT subgroups. MSNA was significantly increased by GTN 400 μg (31 \pm 7 to 41 \pm 6bursts/min, p<0.001) but not by $25\mu g$ (33 $\pm\,9$ to 37 $\pm\,11bursts/min, \,p=0.19)$

Conclusions: The administration of GTN at the dose of 25 μg allows exploring endothelium- independent vasodilation in FMD protocols, inducing only modest hemodynamic and sympathetic responses.

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AN ACUTE BOUT OF PROLONGED SITTING IMPAIRS ENDOTHELIAL FUNCTION AND INCREASES PLASMA CONCENTRATIONS OF ENDOTHELIN-1 IN OVERWEIGHT/OBESE ADULTS: IMPLICATIONS FOR GLUCOSE AND INSULIN METABOLISM

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