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P10.05: CALCIUM CHANNEL BLOCKERS USE IS ASSOCIATED WITH A BETTER COGNITIVE PERFORMANCE IN OLDER HYPERTENSIVE PATIENTS WITH SUBJECTIVE MEMORY COMPLAINTS

G. Watfa, P. Rossignol, A. Kearney-Schwartz, R. Fay, S. Bracard, J. Felblinger, J.M. Boivin, P. Lacolley, F. Zannad, A. Benetos

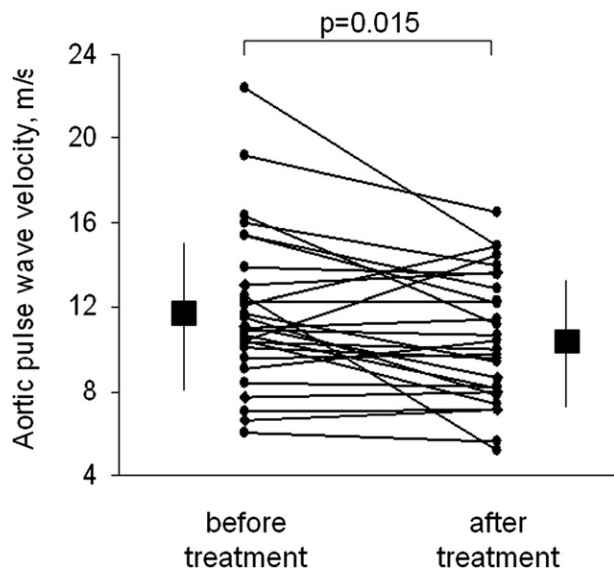
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corrected for a heart rate of 75 bpm decreased from 0.34 ± 0.07 to 0.29 ± 0.08 ($p < 0.01$).

Conclusions: Polymyalgia rheumatica is associated with increased aortic stiffness, which may improve upon reduction of systemic inflammation determined by treatment with corticosteroids.



P10.02
EFFECT OF ANTIHYPERTENSIVE TREATMENT ON AORTIC STIFFNESS IN A GENERAL POPULATION

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Objective: Aortic stiffness, an independent cardiovascular risk factor, is strongly related to age and mean arterial pressure (MAP). In a general population, we investigated effect of antihypertensive treatment on aortic pulse wave velocity (aPWV) with respect to age and MAP.

Design and Methods: In a Czech post-MONICA study, we measured aPWV in 1007 subjects, mean age 54.5 years, 55.0% women, 33.8% on antihypertensive medication. We used linear regression analyses to assess effect of antihypertensive treatment on aPWV. As independent covariates we considered: sex, age (MAP), heart rate, body mass index, smoking, and observer.

Results: Subjects using antihypertensive treatment were older, had higher SBP, BMI and aPWV ($P < 0.0001$). In analysis adjusted for MAP, but not in unadjusted analysis, use of antihypertensive medication diminished effect of age on aPWV (regression equations, untreated subjects (TRT-0): $5.74 + 0.032 \cdot \text{age}$ vs. treated patients (TRT-1) $9.24 - 0.004 \cdot \text{age}$; difference of slope, $F = 28.9$; $P < 0.0001$). In both unadjusted (regression equations $-1.80 + 0.096 \cdot \text{MAP}$ vs. $6.38 + 0.026 \cdot \text{MAP}$; difference of slopes, $F = 28.7$; $P < 0.0001$) and analysis adjusted for age ($3.81 + 0.037 \cdot \text{MAP}$ vs. $9.55 - 0.0056 \cdot \text{MAP}$; difference of slopes, $F = 38.9$; $P < 0.0001$), use of antihypertensive treatment was associated with smaller increase of aPWV with MAP.

Conclusions: In a general population, we observed that use of antihypertensive medication reduce an increase of aPWV with age. The increase of aPWV with blood pressure was also smaller in treated patients compared to untreated subjects. Antihypertensive drugs prevent aortic stiffening even in subjects whose blood pressure is not well controlled.

P10.03
ACTIONS OF VERAPAMIL IN PRODUCING VASCULAR RELAXATIONS

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We have investigated the vascular relaxant actions of verapamil in comparison with the L-type calcium antagonist nifedipine and the putative selective T-type calcium antagonists NNC 55-0396, mibefradil and

thalidomide. Male Wistar rats (250g) were killed by CO₂ overdose, the aorta and vas deferens were removed for organ bath studies and rings of tail artery were set up in small vessel myographs. In rat aorta, verapamil (100 μM) significantly reduced the maximum contraction to noradrenaline to a similar degree as nifedipine or mibefradil, but thalidomide had no effect. In rat tail artery, verapamil (1-10 μM) inhibited contractions to calcium restoration both in the presence of phenylephrine and KCl, but the T-type calcium channel blocker NNC 55-0396 (100 μM) inhibited contractions to calcium restoration only in the presence of phenylephrine, and the L-type blocker nifedipine (10 μM) inhibited contractions to calcium restoration only in the presence of KCl. Verapamil inhibited nerve-evoked contractions of epididymal, but not prostatic, portions of rat vas deferens, an action shared with the T-type calcium channel blocker NNC 55-0396 and by thalidomide. In contrast, nifedipine inhibited contractions of prostatic portions of rat vas deferens. It is concluded that verapamil produces vascular relaxations by a mechanism that involves aspects of both L-type and T-type calcium channel block.

P10.04
VACCINATION AGAINST INFLUENZA A/H1N1 VIRUS ADVERSELY AFFECTS ENDOTHELIAL FUNCTION, BUT NOT ARTERIAL STIFFNESS, IN HIV INFECTED PATIENTS

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Purpose: Vaccines have been shown to induce a transient impairment of endothelial function and arterial elastic properties. Newly developed vaccines against the pandemic influenza A/H1N1 virus have been reported to have a safe cardiovascular profile; however, their impact on endothelial function and arterial stiffness has not been established.

Methods: We recruited 25 HIV infected patients (all male, 3 naïve to antiretroviral therapy, mean age 35 ± 10 years) with a good functional status (mean CD4 count: 719 ± 273). All were free from overt cardiovascular disease; 14 patients were vaccinated with a single dose of a monovalent, adjuvanted vaccine against influenza A/H1N1.11 patients were subjected to a sham procedure (controls). Measurements were taken prior to, 8 and 48 hours post vaccination. FMD of the brachial artery was used as an index of endothelial function; carotid-femoral PWV as a measure of arterial stiffness. ADMA, IL-6 and sICAM-1 were measured in blood samples. Comparisons were performed by repeated measures ANOVA.

Results: Vaccination led to a significant impairment of endothelial function, denoting a diminished bioavailability of nitric oxide that persisted even after 48h (baseline: $6.5 \pm 4.8\%$, 8h: $2.3 \pm 4.9\%$, 48h: $1.8 \pm 4.8\%$; $p = 0.05$). However, arterial stiffness, as assessed by cfPWV, was not significantly altered (baseline: 7.2 ± 1.2 m/sec, 8h: 7.0 ± 1.2 m/sec, 48h: 6.8 ± 0.9 m/sec; $p = \text{ns}$). ADMA, IL-6 and sICAM-1 levels did not change.

Conclusion: Vaccination against influenza A/H1N1 with a monovalent, adjuvanted vaccine leads to endothelial dysfunction in HIV patients, which lasts for at least 48 hours. Given the increased cardiovascular risk of these patients, these findings warrant further research.

P10.05
CALCIUM CHANNEL BLOCKERS USE IS ASSOCIATED WITH A BETTER COGNITIVE PERFORMANCE IN OLDER HYPERTENSIVE PATIENTS WITH SUBJECTIVE MEMORY COMPLAINTS

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Background: Hypertension is strongly associated with cognitive decline and a promising target for dementia prevention. Our aim was to investigate the association between different antihypertensive treatments and cognitive performance in elderly hypertensive patients presenting with subjective memory complaints (SMC).

Patients and methods: 378 elderly hypertensive patients > 60 years (mean age 70.4 ± 6.3 years) treated with at least one antihypertensive agent and presenting with SMC but without dementia were prospectively recruited and underwent a combination of neuropsychological tests, a brain magnetic resonance imaging with semi-quantification of White Matter Hyperintensities (WMH), carotid echotracking, brachial endothelial function and ambulatory blood pressure (BP) assessments.

Results: None of the 3 composite scores (Memory score, verbal fluency, visual memory capacity) was found associated with BP levels. On the other hand, age and gender-adjusted analyses showed a significant and positive association between memory score and calcium channel blockers (CCBs) use (users: $+0.14 \pm 0.09$ versus non-users: -0.12 ± 0.06 , $p = 0.016$). Multivariate analyses also revealed that CCBs use was significantly associated with a better memory score, independently from age, male gender, WMH and carotid wall cross-sectional area, all of which were associated with worse memory scores.

Conclusions: In elderly hypertensive treated patients with SMC, CCBs use was associated with better memory performances independently of BP level and macro and microvascular alterations, suggesting a specific neuroprotective effect of this pharmacological class. Interventional controlled trials are required to confirm the specific protective effect of CCBs on cognitive decline.

P10.06

RESPONSES OF THE AMBULATORY ARTERIAL STIFFNESS INDEX AND OTHER MEASURES OF ARTERIAL FUNCTION TO ANTIHYPERTENSIVE DRUGS

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Objective: We used antihypertensive drugs as pharmacologic tools to clarify the physiologic meaning of the ambulatory arterial stiffness index (AASI) in comparison to pulse pressures (PP), the arterio-ventricular coupling index (AVCI), and aortic pulse wave velocity (aPWV).

Methods: After a 4-week placebo period, 94 and 107 patients with uncomplicated hypertension were randomly assigned to treatment for one year with atenolol 50 mg/d (AT) or perindopril/indapamide 2/0.6 mg/d (PER/IND). From the individual readings in each patient's 24-hour ambulatory BP recording, we determined 24-hour systolic and diastolic BP. We computed PP as the difference between 24-hour systolic and diastolic BP, AASI as unity minus the regression slope of diastolic on systolic BP, and AVCI as $(T/\tau)/(1+2T/3\tau)$, where T is the heart period in seconds and τ is the decay time of aortic BP during diastole.

Results: Compared to PER/IND, in patients on AT, systolic BP and PP decreased less and AVCI lengthened more ($P \leq 0.009$), whereas the changes in AASI and aPWV did not differ between the two treatment groups ($P \geq 0.25$). In patients with the metabolic syndrome (NCEP-ATPIII criteria), AT and PER/IND lowered systolic BP similarly, but AT lowered diastolic BP more than PER/IND. Conversely, in patients without the metabolic syndrome, PER/IND lowered systolic BP more than AT, but diastolic BP to a similar extent.

Conclusions: On antihypertensive drugs with a different hemodynamic profile, AASI and aPWV behaved similarly. The metabolic syndrome seems to modulate the impact of antihypertensive drugs on systolic BP and PP.

P10.07

PERINDOPRIL THERAPY IMPROVES ENDOTHELIAL FUNCTION AND ARTERIAL STIFFNESS IN HEART FAILURE WITH PRESERVED SYSTOLIC FUNCTION

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Background: Number of heart failure patients with preserved systolic function increases with every year, vascular load is one of the leading determinants in ventriculo-vascular coupling and ventricular function.

Aim: to assess endothelial function by photoplethysmography and arterial stiffness on perindopril therapy in HF patients with preserved systolic function.

Methods: 50 patients with exertional dyspnoe were included in the study, I-II NYHA, EF>45%, etiology of HF - hypertension, aged $62.3(\pm 8.4)$, female 56%, BMI 29.9 kg/m^2 . Arterial stiffness was measured by applanation tonometry (Sphygmocor): carotid-femoral PWV and MAP, central pulse pressure (PP), aortic augmentation index (AIX); endothelial function was assessed by photoplethysmography using low arm occlusion, clinical status with MQLHF and 6-minutes walk-test (6MWT) at baseline and in 12-months. All patients were on perindopril therapy, start dose 4mg, mean dose 8 mg.

Results: 12-months therapy resulted in improvement of endothelial function, decreasing of arterial stiffness, clinical improvement. PWV decreased from 10 (8,6;11,9) to 8,8(8,1;11) ($p=0,05$); endothelial function improved from 1,25[1,09;1,52] to 1,42[1,2;1,64] ($p<0,05$), parameters of central hemodynamics changed: MAP from 105,5 (97,5;115,5) to 102(97;106) mmHg; CSBP from 145(132;152) to 130(122;138)mmHg; CDBP from 85 (79;93) to 80 (79;87)mmHg; AIX from 29,5[24,5;34,5] to 28[22;32]. Clinical status: NYHA FC from 2(1;2) to 1(1;1), MQLHF from 39,5(27;47) to 32 (24;39), 6MWT from 390(375;420) to 460(450;470).

Conclusions: 12-months perindopril therapy improved endothelial function, led to reduction of arterial stiffness and resulted in improvement of clinical status of diastolic HF patients, that suggests that perindopril should be considered therapeutically useful in diastolic HF treatment.

P10.08

THE BRACHIAL ARTERY ENDOTHELIAL FUNCTION UNDER THE INFLUENCE OF VASOACTIVE ANTIHYPERTENSIVE TREATMENT

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Objective: To investigate and compare the endothelium-dependent vasorelaxation dynamics when administering beta-blockers carvedilol, nebivolol and calcium antagonist amlodipine to patients with essential arterial hypertension (AH)

Methods: Ninety patients with 1-2 grades AH aged 30-55 years were studied. All patients were randomized to receive carvedilol ($n=45$), nebivolol ($n=25$) and amlodipine ($n=25$) in initial daily doses of 25, 5 and 5 mg respectively. In two weeks if office BP level of 140/90 mmHg was not attained the dose of medicine was doubled. In four weeks in cases of uncontrolled AH the indapamide 1.5 mg was added. The length of administering period was 8 weeks. Endothelial function (EF) was evaluated with the help of flow mediated dilation (FMD) test. The ambulatory BP monitoring (ABPM) was held.

Results: An average daily dose of carvedilol, nebivolol and amlodipine amounted to 31.4 ± 16.2 , 5.7 ± 2.4 and 6.4 ± 2.6 mg. Mean 24-h systolic and diastolic BP significantly decreased in all groups. We also observed that the degree of brachial artery FMD reliably increased by +5.5%, +1.6% and +4.6% under the influence of carvedilol, nebivolol and amlodipine respectively. At the same time the share of patients with full recovering of EF (brachial artery FMD >10%) increased significantly only in carvedilol group – from 4.5% to 27.3% ($p_{\chi^2}=0.004$).

Conclusion: In hypertensive patients the brachial artery endothelial function significantly increased under the influence of vasoactive antihypertensive drugs carvedilol, nebivolol and amlodipine. The greatest effect on brachial artery flow mediated dilation was observed in carvedilol group.

P10.09

HETEROGENEOUS REACTIONS OF FOREARM LARGE ARTERIES AND RESISTANCE VESSELS TO VERAPAMIL TREATMENT

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Objective: Calcium channel blockers possesses vasodilating action but there is no evidence to our knowledge about vasodilating effect on different arterial vessels. The aim of this investigation was to ascertain the reactions of large arteries and precapillary resistance vessels during treatment with sustained-released Verapamil (Flamon-240 SR, Mepha Ltd).

Design and methods: 30 essential hypertensives (WHO II) aged between 40-65 yrs received 2 months' treatment with Flamon-240 SR 1-2 tablets daily. Blood pressure was determined auscultatory. Cardiac output (CO) and systemic vascular resistance (SVR) were derived from