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P1.10: BENEFICIAL EFFECT OF SEQUENTIAL NEPHRON BLOCKADE OF CENTRAL PRESSURE AND LARGE ARTERY REMODELLING IN RESISTANT HYPERTENSION

H.B. Beaussier, M.B. Briet, F.M. Michael, G.B. Bobrie, S.P. Peyrard, P.F.P. Plouin, S.L. Laurent, M.A. Azizi, P.B. Boutouyrie

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creatinine may indicate subclinical organ damage with a greater risk of cardiovascular disease.

P1.08

DETERMINANTS OF VASCULAR DAMAGE IN SYSTEMIC LUPUS ERITHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) is associated with increased cardiovascular risk and early vascular aging. The aim of the study was to evaluate aortic and carotid stiffness, central blood pressure (BP) and wave reflection in women with SLE, in order to identify whether different vascular districts are similarly influenced by disease duration, activity and organ damage.

Methods: Medical and pharmacological history were collected. Disease activity and organ damage were evaluated by ECLAM e SLICC/ACR-DI scores, respectively. Pulse Wave Velocity (PWV) and Augmentation Index (AI) were acquired by applanation tonometry, whereas carotid intima-media thickness (IMT) and stiffness were obtained by an automated image analysis system.

Results: 46 SLE women were enrolled (age 41±10years, BP 116±16/76±9 mmHg). Mean disease duration was 17±9years, ECLAM 0,9±1, SLICC 0,9±1,5. PWV(7,4±1,5 m/s) was related to age (r=0.52, p<0,001), mean BP (r=0.59, p<0.001), SLICC (r=0.44, p=0,01). AI (22,5±10,6%) was related to age (r=0.58,p<0,001), mean BP (r=0.50,p<0.001), SLICC (r=0.60,p<0,001), cumulative corticosteroid dose (CCD,r=0.40,p=0.03). Carotid IMT was related only to age (r=0.45, p=0.006). Carotid stiffness was related to age(r=0.68,p<0.001), AI (r=0.54,p<0.001), disease duration (r=0.45,p<0.03), CCD (0.52, 0.01). In multiple regression models adjusted for confounders, SLICC remained an independent predictor of PWV (p=0.04,r²=0.13) and AI (p=0.04, r²=0.16). Conversely, CCD (p<0.001,r²=0.25) and SLICC (p=0.02,r²=0.01) were independent predictors of carotid stiffness.

Conclusions: In a cross-sectional analysis of a cohort of SLE patients, increased arterial stiffness and wave reflection are independently associated with disease-specific organ damage, but not with disease activity or duration; carotid stiffness is also selectively compromised by chronic corticosteroid use.

P1.09

MILD COGNITIVE IMPAIRMENT IS ASSOCIATED WITH SYSTEMIC VASCULAR DYSFUNCTION

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Aim: To evaluate vascular function and structure in subjects with mild cognitive impairment (MCI).

Methods: 58 MCI and 22 controls (age 74±5vs75±4years, men 45vs59% p=ns) were recruited. Endothelial function in the brachial artery (BA) was studied by flow-mediated dilation (FMD) and response to glyceryl trinitrate, (GTN), while large artery stiffness was measured as carotid-femoral pulse wave velocity (PWV).

Results: MCI and controls had a similar prevalence of established CV disease (14vs13%,p=ns) and traditional CV risk factors (hypertension 50vs54%, diabetes 13vs5%, dyslipidemia 28vs48%, smoking 4vs9%, p=ns for all). MCI showed higher blood pressure (BP) values than controls (pulse pressure 70±16vs62±12mmHg, mean BP 97±9vs91±8 mmHg, p<0.05 for both). PWV tended to be higher in controls compared to MCI (11.0±2.2vs9.9±2.4 m/s, p=0.07) but the difference was not significant after considering mean BP as covariate. MCI and controls showed similar BA diameter baseline shear rate (SR) and response to GTN. In MCI hyperemic SR and SR area under the curve were significantly lower (1591±831vs1175±673s⁻¹, 29.7±15,8*10³vs 21.1±14.9*10³, p<0.05 for all) and time to peak was delayed compared to controls (50±16 s59±16s, p<0.05). Mean FMD values, allometrically corrected for baseline BA diameter, were significantly reduced in MCI (4.5±2.9vs2.7±2.9%, p<0.01). The difference remained significant after considering age, mean BP, and SR area under the curve as covariates (p<0.01).

Conclusions: Patients with MCI showed a significant reduction in conduit artery endothelial function as well as in microcirculatory function. These data

support the hypothesis that impaired systemic vascular function might hamper cognitive function.

P1.10

BENEFICIAL EFFECT OF SEQUENTIAL NEPHRON BLOCKADE OF CENTRAL PRESSURE AND LARGE ARTERY REMODELLING IN RESISTANT HYPERTENSION

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Objective: We have previously shown that combined renin-angiotensin system blockade (RB) was less effective than sequential-nephron blockade (SNB) for controlling BP in resistant hypertension (RH). Whether this is accompanied with an improvement in the mechanical properties of large arteries is unknown.

Design and method: Pts with daytime ambulatory SBP/DBP (dASBP/dADBP) >135 and/or 85 mmHg, despite 4 week with irbesartan (Irb)+HCTZ+amlodipine, were randomised to SNB (n=82) or RB (n=82) for 12 weeks. Central pulse pressure (CPP) and carotid-femoral pulse wave velocity (PWV) were measured by applanation tonometry. High-resolution echotracking system (Walltrack[®]) was used to measure carotid artery diameter (Dcca), wall thickness (WT), circumferential wall stress (CWS), and stiffness. All parameters were measured at baseline and week 12.

Results: Baseline clinical characteristics did not differ between groups. dASBP decreased more in SNB (-19±12 mmHg) vs RB (-8±13 mmHg, p<10-6), either for CPP [SNB (-12.8±16.9 mmHg) vs RB (-1.0±9.3 mmHg, p<0.006)] after adjustment on baseline CPP and delta MeanBP. CCA stiffness and PWV decreased similarly in both groups. Dcca decreased more in SNB (-267±46 µm) vs RB (-7.8±39 µm, p=0.01) after adjustment on baseline D and delta ASBP. WT did not differ and CWS decreased more in SNB (-15.2±16.5 kPa) vs RB (-5.2±12.6 kPa, P=0.001).

Conclusions: In RH pts, a ttt strategy based on SNB improved CPP to a greater extent than a RB strategy. This may lead to a better target organ damage prevention and CV outcome. SNB improved CWS. Whether this effect is due aldosterone blockade or sodium depletion remains to be investigated.

P1.11

TRUE ANTIHYPERTENSIVE EFFICACY OF SEQUENTIAL NEPHRON BLOCKADE IN PATIENTS WITH RESISTANT HYPERTENSION AND CONFIRMED MEDICATION ADHERENCE

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Objective: We previously showed that sequential-nephron blockade (SNB) was more effective than combined renin angiotensin system blockade (RB) for controlling BP in patients with resistant hypertension (RH). We assessed medication adherence (MA) on the antihypertensive (AHT) response to SNB/RB with a new combined scoring system.

Design and method: Pts with daytime ambulatory SBP/DBP (dASBP/dADBP) ≥135 and/or 85 mmHg, despite 4 week with irbesartan (Irb)+HCTZ+amlodipine, were randomised to SNB (n=82) or RB (n=82) for 12 weeks. MA was scored as: (i) plasma Irb concentration; (ii) urinary AcSDKP/creatinine ratio (UR); (iii) last medication intake before visit (LMI); and (iv) pill counting (PC, %). 1 point of MA score was attributed to Irb >20ng/ml, UR >4nmol/mmol, LMI <24h, PC >80%. MA was defined as low (LMA, score ≤2), intermediate (IMA, score =3), and optimal (OMA, score =4).

Results: Among 164 pts: 82 had OMA (46 SNB/36 RB), 52 IMA (23 SNB/29 RB) and 30 LMA (13 SNB/17 RB) (NS). LMA pts were younger than SAs pts (50±11 vs. 56±10 yrs, p<0.011). In OMA pts, the difference in dASBP/dADBP between SNB vs RB was significant (-11 [-17 ; -6]/-6 [-9 ; -2] mmHg, p<0.0001/p=0.0025), favoring SNB, whereas in LMA pts the difference between the two groups did not reach significance (-6 [-19 ; 7]/-1 [-10 ; 7] mmHg, p=0.352/p=0.7096).