

ORAL SESSION

ORAL SESSION 7B

THERAPEUTIC ASPECTS

7B.01 FINAL ANALYSIS ON ADHERENCE TO ANTIHYPERTENSIVE MEDICATION IN TREATMENT RESISTANT HYPERTENSION (TRH) UNDERGOING RENAL DENERVATION (RDN)

R.E. Schmieder¹, C. Ott¹, R. Veelken¹, A. Schmid², M. Uder², S.W. Toennes³.
¹ Universitätsklinikum Erlangen, Nephrology and Hypertension, Erlangen, GERMANY, ² Universitätsklinikum Erlangen, Diagnostic Radiology, Erlangen, GERMANY, ³ Department of Forensic Toxicology, Institute of Forensic Medicine, Frankfurt, GERMANY

Objective: Adherence to medication has been repeatedly proposed to represent a major cause of TRH and may affect the BP response to antihypertensive interventions. We assessed adherence rates in patients with TRH at baseline and 6 months after RDN and the potential impact BP response.

Design and method: 80 patients with TRH have been included in two prospective observational follow-up studies (clinicaltrials.gov, NCT01442883 and NCT01687725) that focus on potential antihypertensive and nephroprotective effects of renal denervation (RDN). After ethical approval on 23.08.2013 we retrospectively approached each patient to give us informed consent for analyzing urine samples that had been collected at baseline and 6 months after renal denervation for toxicological urine analysis (by liquid chromatography-mass spectrometry analysis (LC-MS)) of antihypertensive compounds or metabolites. In addition to office BP, 24-h ambulatory BP (ABP) (Spacelab) and central hemodynamics (Sphygmocor) were assessed as well.

Results: Informed consent was obtained in 79 patients (mean age 60.4 ± 10 years (ABP: $155 \pm 14/88 \pm 13$ mmHg). All meds were detected at baseline in N=44 or 56 % [6 month after RDN: in N=52 or 66%] 1 med was missing in N=22 or 28% [N=17 or 22%], >=2 meds in N=13 or 16% [N=10 or 13%] of whom N=3 did not take any meds at all ($p=0.049$) and central systolic pressure ($p=0.012$) was higher in non-adherent patients ($p=0.049$). A shift analysis revealed that adherence remained the same in 47 subjects (in 35 Ss all meds, in 6 Ss 1 med missing and in 6 Ss >=2 meds missing), whereas in 21 Ss adherence increased and in 11 Ss decreased after RDN. Adherence did not significantly change (Mc Nemar-Bowker Test, $p=0.362$). The decrease in 24-h ABP was not different in those taking all medication at 6 months visit (-7 ± 13 mmHg) compared to those with an increased (-10 ± 13 mmHg) and decreased adherence (-7 ± 14 mmHg) (all $p > 0.20$).

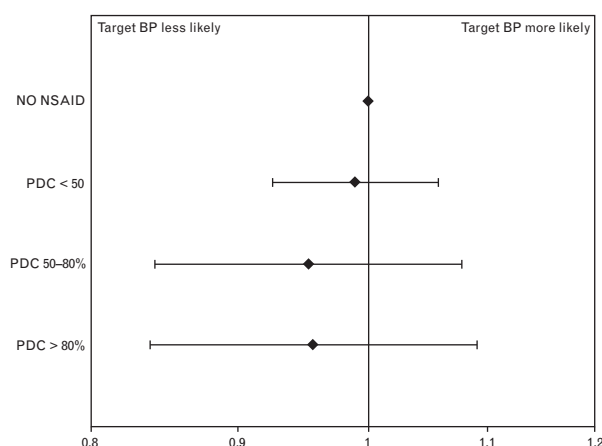
Conclusions: In our tertiary referral center in Northern Bavaria, Germany, non-adherence to medication in patients with TRH was relatively low. Adherence pattern did not change significantly and had no impact on the overall reported BP changes after RDN.

7B.02 THE ASSOCIATION BETWEEN NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND BLOOD PRESSURE CONTROL IN HYPERTENSIVE PATIENTS AND THE RELATION TO GENDER

C. Ljungman¹, T. Kahan², L. Schiöler³, B. Wettermark^{4,5}, K. Bengtsson Boström⁶, J. Hasselström⁷, K. Manhem¹. ¹ Institute of Medicine, Department of Molecular and Clinical Medicine/Cardiology, Sahlgrenska University Hospital, Gothenburg, SWEDEN, ² Karolinska Institutet, Department of Clinical Sciences, Danderyd Hospital, Division of Cardiovascular Medicine, Stockholm, SWEDEN, ³ Institute of Medicine, Section of Occupational and Environmental Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, SWEDEN, ⁴ Centre for Pharmacoepidemiology, Department of Medicine, Karolinska Institutet, Stockholm, SWEDEN, ⁵ Public Healthcare Services Committee, Stockholm

County Council, Stockholm, SWEDEN, ⁶ R&D Centre Skaraborg Primary Care, Skövde, SWEDEN, ⁷ Karolinska Institutet, Department of Neurobiology, Care Sciences and Society, Centre for Family Medicine, Stockholm, SWEDEN

Objective: Approximately 25% of hypertensive patients >65 years are treated for arthrosis, which is the most common cause of long term use of non-steroidal anti-inflammatory drugs (NSAID). NSAID inhibits prostaglandin synthesis and interacts with the renin angiotensin system. The objective of this study was to investigate if concomitant use of NSAID in hypertensive patients is associated with a lower possibility to reach target blood pressure <140/90 mm Hg, and to elucidate if there are gender differences regarding this matter.



Design and method: This cross-sectional cohort study includes 40825 patients with hypertension from the Swedish primary Care Cardiovascular Database (SPCCD) in 2007-2008. Patient characteristics, antihypertensive drug class, dispensations of NSAIDs, comorbidities and blood pressure measurements were analyzed. The proportion of days covered (PDC) with prescription was calculated in order to analyze the NSAID use and the PDC was grouped <50%, 50-80% and >80% of days covered with prescription during 180 days prior to the last blood pressure measurement.

Results: In all 6700 patients had at least one prescription of NSAID. Patients with NSAID were younger (67.9 ± 11.2 vs 69.4 ± 11.9 years, $p < 0.0001$), and more often female (63.2 vs 56.3%, $p < 0.0001$) with a diagnosis of musculoskeletal disease (20.8 vs 12.8%, $p < 0.0001$ and with no cardiovascular comorbidity (26.5 vs 32.1%, $p < 0.0001$). There was no difference in SBP between patients with and without NSAID (142 ± 16 , 142 ± 17 mmHg respectively, ns). Patients with NSAID had a higher DBP (80 ± 10 , 79 ± 10 mmHg, respectively $p < 0.001$). In a logistic regression model adjusted for age, smoking, cardiovascular comorbidity, antihypertensive drug class, education, and country of birth there was no difference in the proportion achieving target blood pressure in patients with and without concomitant use of NSAID irrespective of the PDC for NSAID users (figure 1). The results were similar in both genders.

Conclusions: Concomitant use of NSAID in hypertensive patients does not seem to be associated with a higher blood pressure level. The use of NSAIDs is not associated with a reduced ability of achieving target blood pressure. Thus, hypertensive patients do not a priori need to be discouraged to use NSAID.

7B.03 SAFETY OF BETA-AGONISTS WITH DIFFERENT DURATION OF ACTION IN PATIENTS WITH ARTERIAL HYPERTENSION AND BRONCHO-OBSTRUCTIVE DISEASES

I. Dolgusheva¹, O. Agapova², K. Zykov², O. Sivacova¹, P. Golitsyn¹, I. Chazova¹. ¹ Russian Cardiology Complex, Department of Hypertension, Moscow, RUSSIA, ² Moscow State University of Medicine and Dentistry named after A.I. Evdokimov, Laboratory of Pulmonology, Moscow, RUSSIA

Objective: To evaluate the safety of beta-agonists (BA) with different duration of action (short-acting (SABA), long-acting (LABA), ultra-long-acting (ULABA) in patients with arterial hypertension (AH) and chronic obstructive pulmonary disease (COPD) or bronchial asthma.

Design and method: 40 patients with AH and COPD (gr.1) and AH and asthma (gr.2) were enrolled and examined initially. At the next three month patients were treated with 3 types of BA: at the 1st month – with salbutamol (SABA), at 2nd month –with formoterol (LABA), at 3rd month –with indacaterol (ULABA). Initially, after one week and at the end of each month blood pressure (BP) and heart rate (HR) on the visit, serum potassium in blood, electrocardiogram, were evaluate. After one week and at the end of three month of treatment with BA all patients underwent Holter monitoring and ambulatory blood pressure 24-monitoring (ABPM). Results are presented as Mean ± sd.

Results: Patients were 64 ± 7.7years (22-male,18-female), with BMI 29.8 ± 5.3 kg/m2; BP in gr.1 was 128.4 ± 14.3/81.1 ± 19.7 and 135 ± 13/83 ± 9.9 mmHg in gr.2, p=NS, initially. Baseline, 1-month, 2-month, 3-month BP and HR levels on the visit were similar among all patients (p=NS). At the end of the third month of treatment with BA different duration of action in gr.1 daily average Systolic BP (SBP) was lowered than initially (129 ± 10.2 vs 124 ± 10.5, p<0.05). On the contrary in gr.2 daily average SBP became increased than initially (122 ± 14.1 vs 127 ± 16, p<0.05).Treatment with BA caused significant serum potassium change in blood in both group: in gr.1 initially was 4.5 ± 0.5 mmol/l, after SABA use - 4.2 ± 0.4(p<0.05), LABA- 4.1 ± 0.4(p=NS), ULABA-4.2 ± 0.4(p<0.05); in gr.2 initially was 4.4 ± 0.4 mmol/l, after use SABA- 4.1 ± 0.3(p<0.05), LABA- 4.3 ± 0.3(p=NS), ULABA- 4.15 ± 0.6(p<0.05). In gr.2. three patients had hypokalemia.

Conclusions: Treatment with BA in patients with AH and bronchoobstructive diseases significantly decreased levels of serum potassium in the blood in both group and led to reduction of daily average SBP and in contrast treatment of patients with AH and asthma resulted in increasing of daily average SBP. Our results suggested the need for a different treatment of patients with AH and COPD or asthma.

7B.04 EFFECT OF SERTRALINE IN PAROXYSMAL HYPERTENSION

J. Vaclavik¹, A. Krenkova², E. Kocianova¹, T. Vaclavik³, M. Kamasova¹, M. Taborsky¹. ¹ Department of Internal Medicine I, Cardiology, University Hospital Olomouc and Palacký University, Olomouc, CZECH REPUBLIC, ² Faculty of Medicine and Dentistry, Palacký University, Olomouc, CZECH REPUBLIC, ³ Faculty of Informatics and Statistics, University of Economics, Prague, CZECH REPUBLIC

Objective: Paroxysmal hypertension or pseudopheochromocytoma is a quite common problem in clinical practice. Anxiety or panic disorder may be one of the major causes. Optimal treatment for this condition is not established.

Design and method: Between April 2008 and October 2014 we prospectively enrolled 70 patients referred to our department for symptomatic paroxysmal hypertension. Patients received sertraline (a selective serotonin reuptake inhibitor, 50 mg once daily) as an add-on to their current medication. Effect of this treatment was assessed on next clinical visit at least 3 months later.

Results: Of the 70 enrolled patients, 58 (83%) had also sustained arterial hypertension. Mean office baseline blood pressure (BP) was 146.7/84.3 mmHg and patients used mean 3.0 antihypertensive drugs. 19 patients (27%) were not using sertraline on next clinical visit (6 did not start using sertraline, 10 withdrew because of side effects, 3 were lost to follow-up). Of the remaining 51 patients who were using sertraline on next clinical visit, 46 (90%) reported good effect of this treatment. Symptoms of paroxysmal hypertension fully subsided in 31 (61%) and were partially reduced in 15 (29%). Mean office BP in patients using sertraline decreased by 13.8/8.5 mmHg (P<0.001 for both).

Conclusions: Sertraline effectively takes away or reduces symptoms of paroxysmal hypertension in majority of patients who use and tolerate this treatment.

7B.05 DIFFERENTIAL EFFECTS NEBIVOLOL AND VALSARTAN ALONE AND IN COMBINATION ON 24-HOUR AMBULATORY RATE-PRESSURE PRODUCT, STROKE LOAD, AND BLOOD PRESSURE-HEART RATE VARIABILITY

J. Izzo, O. Saleem, S. Khan, P. Osmond. University at Buffalo, Buffalo, NY, USA

Objective: Beta-blockers are antihypertensive drugs indicated for treatment of cardiomyopathies but little is known about their effects on cardiac workload in the ambulatory setting. We compared the effects of the beta-blocker nebivolol (N), the angiotensin receptor blocker valsartan (V) and combined V/N on 24-hour ambulatory central rate-pressure product (ACRPP, an index of myocardial oxygen consumption rate), stroke load (SL) and blood pressure-heart rate variability (SD and coefficient of variation).

Design and method: Subjects with hypertension (SBP>140 or DBP>90, n=26 including 21 blacks) were studied in a 3-way, double-blind, randomized crossover study. After 4 weeks of each drug (V 320, N 40, or V/N 320/40 mg daily), ambulatory pulse wave analysis (IEM MobilOGraph) was performed every 20 min for 24-hour with primary (ACRPP) and secondary endpoints analyzed by sequential paired t-analysis. SL = ACRPP/heart rate.

Results: The table displays the main results. All 3 treatments resulted in similar brachial and central BP values. Addition of N to V resulted in lower ACRPP: 24-hour and daytime by 11 and 14% (p<0.001 each) and nighttime by 4% (p<0.02). This effect was driven largely by the heart-rate slowing effects of N (by 15–18%, p<0.001 each). SL, however, was lower with V than either N or V/N (about 10%, p<0.001 each). Variability (standard deviation and coefficient of variation) of ACRPP and heart rate were lower with N and V/N than V. Separate analysis of blacks revealed values very similar to those of the entire treatment group.

Conclusions: We conclude that 24-hour ambulatory hemodynamic monitoring is feasible in clinical trials. The rate-slowing effects of nebivolol (both N and V/N) cause lower ambulatory cardiac oxygen consumption compared to V alone but at the same time, N and V/N cause an increase in stroke load. Absolute and relative heart rate variability is higher with V than N or V/N. These results are driven primarily by the effects in blacks.

Valsartan (V)	Valsartan + Nebivolol (V+N)	Nebivolol (N)	P (V vs. V+N)	P (V vs. N)	P (N vs. V+N)
Central rate-pressure product (ACRPP, units)					
2762 (479)	2371 (405)	2446 (397)	0.000	0.002	0.235
Stroke load (units)					
35 (4.6)	39 (3.7)	39 (3.9)	0.001	0.000	0.588
Central systolic blood pressure (mm Hg)					
132 (15)	134 (15)	136 (14)	0.622	0.248	0.487
Brachial systolic blood pressure (mm Hg)					
143 (16)	145 (16)	147 (15)	0.601	0.224	0.578
Brachial diastolic blood pressure (mm Hg)					
88 (12)	87 (13)	89 (12)	0.623	0.56	0.302
Heart rate (beats/min)					
78 (14)	63 (10)	64 (8)	0.000	0.000	0.677

7B.06 ROUTINE URINARY DETECTION OF ANTIHYPERTENSIVE DRUGS FOR ESTIMATION OF ADHERENCE TO TREATMENT: A CROSS SECTIONAL STUDY

I. Hamdidouche^{1,2,3}, V. Jullien^{1,3}, E.M. Billaud^{1,3}, P. Boutouyrie^{1,2,3}, M. Azizi^{1,3}, S. Laurent^{1,2,3}. ¹ Department of Pharmacology, Clinical Investigation Center and Hypertension Unit, Hopital European Georges Pompidou, Paris, FRANCE, ² INSERM U970, Paris, FRANCE, ³ Paris Descartes University, Paris, FRANCE

Objective: Adherence to antihypertensive treatment (AHT) is usually assessed by scales such as Morisky Medication Adherence Scale questionnaire (MMAS-4) but objective urinary drug levels quantification by liquid chromatography mass spectrometry (LCMS-MS) is now available. Our aim was to compare adherence assessed by LCMS-MS or MMAS-4, in patients with resistant hypertension (RH), compared to patients with well controlled hypertension (CH).

Design and method: RH cohort consisted in 82 patients with daytime ABPM > 135/85 mmHg after 4 weeks treatment with a standardised triple AHT participating to a clinical trial. The CH cohort consisted in 91 patients followed in a routine care practice with controlled office BP (<140/90 mmHg) by a median of 2 (range 1–4) AHT. Urinary levels of 14 AHT or their metabolites were evaluated by LC/MS-MS. MMAS-4 was only available in CH. Patients were aware (RH) or not (CH) of the measurement. Non-adherence was defined as a urinary level of at least one AHT below the limit of quantification.

Results: LCMS-MS results: in the RH cohort, 63 patients (77%) were adherent, 11 (13%) were partly non-adherent and 8 (10%) were fully non-adherent. In the CH cohort, 86 (93%) were adherent, 5 (6%) were partly non-adherent, and 1 (1%) was fully non-adherent. Office SBP in the CH cohort was significantly higher in non-adherent (partially or fully) than in fully adherent patients (median: 140 vs. 130 mmHg, respectively; p=0.01). Office DBP did not differ. According to LCMS-MS, the full adherence rate was significantly higher in CH compared to RH cohort (p=0.002). According to MMAS-4 available in 88 CH patients, 76 (86%) were fully adherent, and 12 (14%) were medium or low adherent and no significant difference in office SBP/DBP was observed between the two subgroups. There was low or no agreement between LCMS-MS and MMAS-4, with 15/88 non concordant tests.

Conclusions: In conclusion, measurement of urinary AHT by LCMS-MS gives relevant information on adherence to treatment in patients attending an outpatient clinic. This information is not overlapping with questionnaire tests. It confirms the role of objective non-adherence to treatment in resistance to treatment.