

PP.23.07

ACUTE SILDENAFIL USE LOWER 24H BLOOD PRESSURE LEVELS IN RESISTANT HYPERTENSION A RANDOMIZED, PLACEBO CONTROLLED, CROSS-OVER TRIAL

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Objective: The present study sought to evaluate whether acute administration of sildenafil compared with placebo improves ambulatory BP levels in RHTN subjects.

Design and method: This interventional, single-blinded, placebo-controlled, one-way crossover trial included 26 patients with true RHTN. Increasing oral doses of sildenafil were given at 30 minute-interval (37.5 mg, 50 mg and 100 mg) in a single day. After a washout period of 14 days, patients received consecutive oral doses of placebo and the protocol was repeated. Before and after each protocol day (sildenafil and placebo), patients underwent 24-hour ABPM evaluation.

Results: The reduction of systolic (-8.8 ± 1.4 vs. 1.3 ± 1.2 mmHg), diastolic (-5.3 ± 3.3 vs. 1.8 ± 1.1mmHg) and mean (-7.9 ± 3.6 vs. 0.8 ± 0.9 mmHg) 24-hour BP were higher after sildenafil compared with placebo. The main differences were observed on daytime BP levels (systolic; -6 ± 4.7 vs. 4.4 ± 1.5 mmHg; and mean: -4.8 ± 3.9 vs. 3.5 ± 1.4mmHg; sildenafil vs. placebo, respectively).

Conclusions: Our study suggests that an acute high-dose load of sildenafil improves ABPM parameters in resistant hypertensive patients. Considering its antihypertensive effect, sildenafil may represent a therapeutic option for the treatment of RHTN.

PP.23.08

PREVALENCE OF RESISTANT HYPERTENSION IN THE ELDERLY HYPERTENSIVE SUBJECTS - THE RESULTS OF THE POPULATION-BASED STUDY 'POLSENIOR'

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Objective: The aim of the study was to assess the prevalence of drug-resistant hypertension among Polish elderly population.

Design and method: The cross-sectional, population-based survey PolSenior was performed on random sample of elderly subjects (years: 2007–2011). Of 4979 subjects aged 65 years (range: 65 to 104), 3100 subjects taking the antihypertensive medications or untreated hypertensive subjects with uncontrolled blood pressure (BP = > 140/90 mmHg) were included to the analysis. Resistant hypertension (RHT) was defined as the uncontrolled hypertension despite taking 3 or more medications each one from different drug classes. The used definition of RHT was not include the requirement of a diuretic.

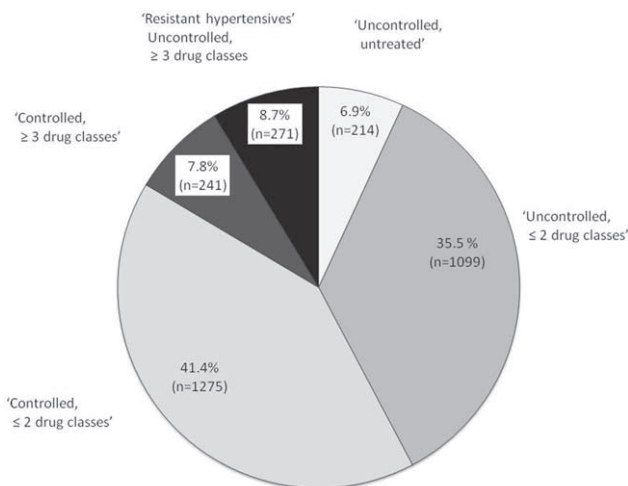


Figure 1. Proportions (and numbers) of subjects in the PolSenior survey with different levels of BP control and treatment intensities.

Results: Mean age of the subjects was 78.8 ± 8.4 yrs, 51.1% were women. The prevalence of RHT was 8.7% (Figure 1) and it tended to be more prevalent in younger than in very old subjects (P for trend = 0.058). Compared with the subjects with controlled hypertension using 3 or more medications from different drug classes, the elderly subjects with RHT tended to be younger (79.3 vs 77.9 yrs, P = 0.053) and much less likely treated with diuretic (51.9% vs 24.7%, P < 0.001). The subjects with RHT did not differ in the proportion of taking a thiazide or thiazide like diuretics but were much rarely treated with an aldosterone receptor antagonists (51.9% vs 24.7%, P < 0.001) or loop diuretics (31.4% vs 18.6%, P < 0.001).

Conclusions: The prevalence of RHT in population seems to be relatively low but it is difficult to estimate it precisely due to the problems with the definition of RHT, clear classification of subjects with hypertension as well as establishing the adherence level in the uncontrolled patients. Nonetheless, our data from the elderly population correspond with the results of the NHANES study 2003–2008), as well as the recently published data from the metaanalysis (Achelrod D. et al. Am J Hypertens 2015). The further analyses are needed to assess the true resistant hypertension with the requirement of usage of diuretic, especially an aldosterone receptor antagonists.

PP.23.09

HYPOTENSIVE EFFICACY AND SAFETY OF EPLERENONE IN PATIENTS WITH RESISTANT ARTERIAL HYPERTENSION

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Objective: The objective of the study was to assess the hypotensive effect and safety of add-on therapy with aldosterone inhibitor – eplerenone – in patients with resistant arterial hypertension.

Design and method: 50 patients with office systolic (SBP) and diastolic blood pressure (DBP) still exceeding 140 mmHg and 90 mmHg respectively, despite being treated with at least 3 hypotensive drugs, including diuretic and who did not have history of aldosterone inhibitors treatment in last 3 months were enrolled to this study. 28 patients with mean blood pressure during daytime greater than 135/85 mmHg, with potassium levels of no more than 5,1 mmol/l and serum creatinine concentration less than 115 umol/l had eplerenone 25 mg or 50 mg daily added to their therapy. Each patient had office blood pressure measurement, ambulatory 24-hour blood pressure monitoring (ABPM) and laboratory tests carried out at the beginning and at the end of the study. Observation time was 6 weeks. 6 patients were excluded from the analysis due to non-compliance.

Results: After 6 weeks of follow-up 18 patients (82%) had reduction of office blood pressure and 17 patients (77%) of ambulatory blood pressure. Mean decrease in office SBP and DBP was 15 and 8 mmHg respectively (95% CIs: 8 to 22 and 4 to 12, p < 0,001). Mean decrease in ABPM during daytime was 9 in SBP and 5 mmHg in DBP (95% CIs: 3 to 15 and 1 to 8, p < 0,01). Mean decrease in ABPM during nighttime was 7 in SBP and 4 mmHg in DBP, but was not statistically significant. There were no statistically significant changes in electrolytes and serum creatinine levels. No patient reached potassium level greater than 5,1 mmol/l or creatinine greater than 115 umol/l.

Conclusions: This study shows that eplerenone is safe and efficient drug when added to the therapy of resistant arterial hypertension.

PP.23.10

CLINICAL IMPACT OF ANGIOTENSIN CONVERTING ENZYME (ACE) POLYMORPHISM ON DEVELOPMENT OF CARDIOVASCULAR AND METABOLIC COMPLICATIONS IN SUBJECTS WITH RESISTANT HYPERTENSION

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Objective: The renin-angiotensin system and endothelial function have been both associated with hypertension, but there are very few data in resistant hypertension. The aim of the present study was to assess the relationship between insertion/deletion polymorphism in the gene encoding the angiotensin-converting enzyme (ACE I/D) and estimation of cardiovascular and metabolic complications in resistant hypertensive patients.

Design and method: In the present study we analyzed and genotyped data from 150 patients with resistant hypertension. We have evaluated arterial stiffness (AS) indices, carotid intima-media thickness (cIMT), HOMA index and clinical data.

Results: D allele was more prevalent, and 74 patients presented DD homozygosis. Sixty-eight patients had metabolic syndrome (MetS), without significant differences between DD and I allele carriers. DD genotype appeared strongly associated with higher HOMA values ($p < 0.001$), and also with both AIx ($p = 0.003$) and PWV ($p = 0.023$). A significant association was found between DD genotype and cIMT ($p < 0.005$), and the presence of carotid plaques ($p < 0.001$). HOMA was correlated with AS (PWV: $p < 0.001$; AIx: $p < 0.01$).

Conclusions: Our results are in agreement with experimental evidences suggesting that DD genotype appeared to be associated with AS, increased cIMT, HOMA index, and the presence of carotid plaques, and confirming that D allele plays an important risk role on development of cardiovascular and metabolic complications in patients with resistant hypertension, independently from the presence of other risk factors.

PP.23.11

MATRIX METALLOPROTEINASE 2 GENE POLYMORPHISM ASSOCIATES WITH RESISTANT HYPERTENSION

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Objective: The lack of blood pressure (BP) control ($>140/90$ mmHg) – even in the presence of three or more antihypertensive drugs of different classes – define the hypertensive patients at high cardiovascular (CV) risk and high incidence of target organ damage (TOD) as resistant hypertensives (RH). Studies suggest the involvement of metalloproteinase 2 (MMP-2) in hypertension and in CV remodeling associated with TOD. Hypertension is a multifactorial condition in which BP heritability and genetic factors may have a large contribution in the development of the disease. MMP-2 single nucleotide polymorphisms (SNPs) have been associated with the predisposition of CV alterations. Few studies have evaluated the impact of MMP-2 polymorphisms on clinical conditions and their influence in RH is unknown. The aim of this study is to analyze the influence of MMP-2 SNPs in RH, as well as their association with TOD in this high CV risk group.

Design and method: 119 RH patients and 136 mild to moderate hypertensives (HT) were included and submitted to clinical and laboratorial evaluations. We assessed genotypes by allelic discrimination assay using real time polymerase chain reaction. We compare clinical and laboratorial characteristics according to SNPs genotypes/haplotypes (rs243865, rs243866 and rs2285053). TOD were categorized by left ventricular mass index (women > 95 g/m² and men > 115 g/m²) and arterial stiffness (PWV >10 m/s).

Results: We did not find association of studied SNPs with TOD and clinical features. However, the allelic and genotype frequencies of rs2285053 showed to be different between RH and HT subjects (C vs T, $p = 0.02$; CC vs CT vs TT, $p = 0.04$, respectively), with high prevalence of C allele in the RH group. Moreover, haplotype frequencies were also different (GCC vs GCT vs ATC, $p = 0.03$) between groups. Finally, regression analysis demonstrated that haplotype was associated with resistance to treatment, as well as age, gender, race, BMI, LVH and aldosterone levels.

Conclusions: We conclude that only the SNP rs2285053 may be associated with RH when compared to controlled counterparts. Our finding suggests that the presence of C allele may have some bearing in the resistance to antihypertensive process.

PP.23.12

OUT-OF-OFFICE BLOOD PRESSURE MEASUREMENT IN PATIENTS WITH RESISTANT HYPERTENSION IN EVERYDAY CLINICAL PRACTICE: STILL A LONG JOURNEY TO GO

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Objective: White coat hypertension (elevated office blood pressure but normal home and/or ambulatory blood pressure) is frequently encountered in resistant hypertension. Current guidelines recommend home or ambulatory blood pressure measurement (ABPM) for all patients with resistant hypertension. The aim of this study was to assess the adoption of these guidelines in every day clinical practice.

Design and method: Our study included 212 sequential patients with resistant hypertension that attended our hypertension outpatient clinic. Patients were asked whether ABPM was performed, or if they had been given advice on systematic blood pressure measurement at home, according to guidelines.

Results: ABPM was performed in 9 patients out of 212 study participants (4.2%). Out of 212 patients only 33 (15.6%) had been advised to measure blood pressure at home, whereas only 14 patients (6.6%) had measured their blood pressure on a regular basis (morning-evening), using a certified sphygmomanometer, according to guidelines.

Conclusions: Poor adoption of guidelines about home or ambulatory blood pressure measurement for patients with resistant hypertension in everyday clinical practice underlines the need for more intensive orientation of physicians managing patients with resistant hypertension.

PP.23.13

ANALYSIS OF ELIGIBILITY CRITERIA FOR RENAL SYMPATHETIC DENERVATION

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Objective: Resistant hypertension (RH) is a rare condition that affects approximately 10% of hypertensive population, it's defined as blood pressure (BP) $> 140/90$ mmHg despite three full doses antihypertensive drugs including a diuretic. True RH is confirmed when pseudo-hypertension, secondary hypertension or poor adherence are excluded. Percutaneous radio-frequency catheter-based renal sympathetic denervation (DRN) is one of the most used invasive treatments for these patients. The goal of the study is to assess the percentage of eligibility to DRN and analyze the exclusion criteria in a group of resistant hypertensive patients.

Design and method: We retrospectively analyzed data of 35 patients (63% female) referred to our Hypertension Unit between June 2011 and June 2014. We considered eligible for DRN subjects with office systolic blood pressure $> = 160$ mmHg and patients with severe hypertension treated with fewer drugs for poly-intolerances/allergies. Secondary hypertension form and white coat hypertension were excluded. Patients with confirmed true resistant hypertension underwent CT angiography in order to check the renal anatomic criteria of eligibility to the DRN.

Results: 35 caucasian patients (63% female) referred to our Hypertension Unit between June 2011 and June 2014 for DRN assessment. At the first evaluation median systolic and diastolic office BP were 179 ± 25 mmHg and 105 ± 20 mmHg; six month later, after appropriate changes in lifestyle and drug therapy, systolic/diastolic office BP was reduced of $18/8$ mmHg ($p < 0.05$). In the most of cases, patients had to BP control with introduction of antialdosteronic (35%). In our sample, 27 patients were considered unsuitable for the DRN for many reason: blood pressure control with optimization of drug therapy (52%), evidence of white coat effect (22%), secondary hypertension (22%), lack of true resistant hypertension (18%), absence of consent to the procedure (29%).

Conclusions: A careful patients selection in Specialistic Center is necessary before DRN; indeed frequently a good BP control is obtained with appropriate drug therapy changes and exclusion of secondary forms.

PP.23.14

CONTROL OF BLOOD PRESSURE AND DIASTOLIC FUNCTION OF LEFT AND RIGHT VENTRICLE IN HYPERTENSIVE PATIENTS

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Objective: The aim of this study was to evaluate diastolic function of right and left ventricles in hypertensive patients and heart rate variability (HRV) according to the control of blood pressure.

Design and method: We examine 103 hypertensive patients: group 1 – 41 newly diagnosed without treatment, group 2 – 31 with controlled hypertension and group 3 – 31 with resistant hypertension, uncontrolled in spite of treatment of more than 3 drugs. We assessed the traditional risk factors, echocardiography and HRV as well as blood pressure using ambulatory blood pressure monitoring. Differences between groups were analysed using one-way ANOVA and post-hoc Tukey test.

Results: Table 1. Characteristics of patients:

Conclusions: Patients with resistant or controlled hypertension did not differ in terms of both diastolic and systolic function of left ventricle or HRV indices in comparison to newly diagnosed. Whereas there were differences between groups (1 versus both 2 and 3) in some indices of right ventricular diastolic function (E/E' , $E't$) even after adjustment to age and blood pressure values.