Sphygmocor and PulsePen, in 68 consecutive patients (59.5 ± 15.7 years) from our cardiovascular department.

**Results:** All hemodynamic variables, including PWV, carotid systolic blood pressure (cSBP) and carotid augmentation index (cAI), measured by the two devices were strongly correlated (R² = 0.637, P < 0.0001). Although compared to Sphygmocor, PulsePen significantly estimated higher PWV, cSBP and cAI by 0.8 ± 1.5 m/s, 4.7 ± 10.2 mmHg and 5.7 ± 10.2 %, respectively, no significant interclass difference was found between the two devices (P > 0.05). Furthermore, high interclass correlation coefficients (ICC > 0.76) were obtained when the two devices were compared, and no significant difference was observed between 1 and slopes of correlation plots of hemodynamic parameters, which varied from 0.888 to 1.010.

**Conclusions:** The significant discrepancies of hemodynamic parameters observed between Sphygmocor and PulsePen were neglectable in the setting of population study, and did not influence the capability of the two device in cardiovascular risk assessment for individual.

**PP.38.496 DIFFERENCES IN BIOAVAILABILITY OF NIFEDIPINE OSMOTIC PUSH-PULL SYSTEMS: PREDICTIVE RESULTS FROM IN-VITRO COMPARED TO IN-VIVO**

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Two similar osmotic push-pull systems were investigated in vitro and compared to in vivo PK data obtained in healthy subjects. Reference contains a bilayer core and Test contains a monolayer core. Identical batches were used for in vitro and in vivo testing of the products having a marketing authorisation in Canada.

In vitro dissolution tests over 24 hours were performed prior to the study. The clinical study was conducted in a 4-period crossover design with 26 subjects. Investigations were performed under fasting or fed conditions. Accumulated 24-hour in-vitro tests were performed using USP paddle apparatus in 900 mL surfactant-containing buffer under sink conditions at 37°C. 12 tablets of each product were investigated. Samples were taken every 60 minutes and nifedipine concentration was determined using HPLC.

After oral administration, blood samples were taken until 48 h post dosing. Quantification in plasma was performed using validated HPLC-MS/MS method. PK parameters were determined model-independently for each treatment directly from measured concentrations.

In vitro profiles of Test and Reference indicated deviations in initial and terminal release of nifedipine with later onset and lower quantity of drug release for Test, which were confirmed by the findings obtained from in vivo investigations. Test showed a delayed onset of absorption consisted with a later achievement of the plateau phase. Parameter for early exposure, AU(t=0-1h), AU(t=0-2h) and AU(t=0-3h) differed between both products by almost a factor of two.

Under fasting condition, Cmax–values obtained were equivalent, but for total exposure, determined as AU(t), 90% confidence intervals for mean ratio Test/Reference surpased acceptance range and bioequivalence could not be shown. Confirmation of bioequivalence was not possible under fed condition, where point estimates indicated a reduction of almost 20% and confidence intervals did not include 100%.

Differences in completeness of delayed onset and drug release from monolayer system as observed in vitro is obviously relevant for in vivo performance. These significant differences may have clinical implications for blood pressure control.

**PP.38.497 EFFECT OF AN EDUCATIONAL INTERVENTION ON WEIGHT AND BLOOD PRESSURE IN OBSESE HYPERTENSIVE PATIENTS. TWO YEARS OF FOLLOW-UP**

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**Objective:** To assess the effect on weight and blood pressure of an educational intervention in obese hypertensive patients.

**Results:** A before-after study was conducted to evaluate the effect of a 12-month educational intervention on weight and blood pressure in obese hypertensive patients. The individualized educational program consisted of: nutrition information, motivation test, individualized portion-controlled diet and reinforcement of information once a month with measurement of weight, waist circumference (WC) and BMI. Measurements of BMI (kg/m2), WC (cm), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were performed at the beginning of the study, one year later (when the educational intervention ended) and two years later.

**Results:** 61 patients were studied (32 men, 29 women), aged 59.84 ± 14.59. BMI decreased in 56 patients (91.8%) and WC in 54 patients (98.5%). The evolution of BMI and WC was: BMI 35.68 ± 3.56, BMI 31.65 ± 4.29, BMI 31.27 ± 3.94. WC 107.36 ± 10.65, WC 104.94 ± 10.94, WC 102.75 ± 10.36. There were differences statistically significant among BMI and WC (average reduction 2.05, ICC% 1.46, 2.59, p < 0.05). BMI and BIM were similar. The average reduction of WC was 3.31 (IC95% 1.94, 4.68), p < 0.05, at one year and 4.61 (IC95% 3.06, 6.17), p < 0.05, at two years. The evolution of SBP, DBP and MAP was: SBP 133.33 ± 15.30, SBP 136.12 ± 16.26, SBP 125.67 ± 15.30, DBP 83.77 ± 8.32, DBP 78.00 ± 8.82, MAP 102.71 ± 10.08, MAP 101.14 ± 11.16, MAP 92.5 ± 11.11. The reduction in blood pressure at one year is not statistically significant, but it reaches statistical significance at two years: average reduction in SBP 12.89 mmHg (IC95% 8.63–17.10) p < 0.05, in DBP 8.30 (IC95% 5.88–10.72) p < 0.05 and in MAP 10.45 (IC95% 7.24–13.67) p < 0.05.

**Conclusion:** An individualized educational intervention in obese hypertensive patients lowers BMI, WC and blood pressure among studied individuals. Waist circumference continues its reduction after concluding the intervention.

**PP.38.498 FURTHER TREATMENT IN UNCONTROLLED HYPERTENSIVE PATIENTS WITH EXFORGE (FUTURE STUDY)**

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**Objective:** To evaluate the efficacy of Exforge® (single-pill combination of amlopine and valsartan) therapy in hypertensive patients who were previously uncontrolled (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg) with amlopine mono- or amlopine based combination therapy. Secondary objectives were tolerability and compliance with Exforge®.

**Patients and Methods:** An open-label, multicenter, non-interventional, observational study, evaluated 3390 consecutive patients (mean age 58.37 ± 12.11 years) at baseline (visit 1) and at weeks 4, 8, 12, 16 (visits 2, 3, 4) and for two years later (visit 6). The administration of Exforge® was done according to the approved prescribing information and dosage left to the discretion of the physician. Vital signs, risk stratification, medical treatment, adverse events, compliance and laboratory parameters (optional) were recorded at each visit. Repeated measures analyses of variance, and Friedman’s or McNemara’s multivariate tests were applied for continuous and categorical variables, respectively. The significance level was 5%.

**Results:** Mean sitting blood pressure was 164.2/94.9 mmHg at baseline, and 131.07/9.8 mmHg at week 12, reflecting a reduction of 33/15 mmHg (p < 0.0001). 75.9% of the total patient population reached the target blood pressure < 140/90 mmHg at week 12. 64.8% of patients reaching this blood pressure target were treated exclusively with Exforge®. The average dose of Exforge® was 6.36 (± 2.13) mg amlopindin/126.26 (± 37.15) mg valsartan.

No clinically relevant changes regarding the laboratory parameters (total plasma cholesterol, LDL-cholesterol, HDL-cholesterol, blood sugar, serum GGT and GPT) and serum creatinine and potassium) were observed during the study. The Exforge® therapy was well tolerated, the most frequent AE was localized oedema (1.9%). Patient compliance to Exforge® therapy reached 94.5% at week 12.

**Conclusion:** Exforge® provides powerful incremental BP reductions in patients uncontrolled on amlopine mono- and amlopine-based therapies with excellent patient compliance and good tolerability.

**PP.38.499 THE INFLUENCE OF DIFFERENT ANTIHYPERTENSIVE DRUGS ON BLOOD PRESSURE VARIABILITY**


**Background:** The exploration of Blood Pressure (BP) variability and of the influence of different antihypertensive drugs on BP variability may improve...
Forty patients, M/F 18/22; age 58 to Nebivolol (-10.35 reduced systolic BP variability during the night time period when compared reducing SBP variability during the night time period. Valsartan significantly but long-term treatment with Valsartan proved to be more efficient in Both Valsartan and Nebivolol decreased 24 h BP variability Results: Both Valsartan and Nebivolol decreased 24h BP variability but long-term treatment with Valsartan proved to be more efficient in reducing SBP variability during the night time period. Valsartan significantly reduced systolic BP variability during the night time period when compared to Nebivolol (-10.35 ± 3.01 mmHg vs. 6.27 ± 4.26 mmHg, p < 0.05).

Conclusions: Treatment with ARBs (Valsartan) and BBs (Nebivolol) efficiently reduces the BP variability during the day and night period of time as first line antihypertensive agents. Valsartan significantly reduces systolic BP variability during the night time period when compared to Nebivolol. Antihypertensive treatment using long acting agents like an angiotensin receptor blocker or an ultraselective beta blocker could offer a better cardiovascular protection by reducing the BP variability.

**PP.38.501 A FUNDAMENTAL RELATIONSHIP BETWEEN BLOOD PRESSURE DISPERSION AND ARTERIAL PROPERTIES**

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Evidence shows that blood pressure (BP) variability may depend on mean BP and possesses prognostic significance. Using model approach this study aimed to show that the known increase of arterial stiffness at greater pressures is a mechanism that couples average BP to variability. The 'static' mechanical properties arteries in situ is characterized by the variation of arterial pressure P in response to changes in blood volume V (or arterial diameter), as illustrated in Figure A. On this P-V curve arterial stiffness at a reference point (e.g. at the systolic BP (SBP) or diastolic BP (DBP)) is represented by the slope of the curve that becomes steeper at higher pressures. Such P-V 'curving' actually transforms volume variations with increasing amplitude (3 values are shown), but having the same mean value, into corresponding pressure variations with mean value that increases for greater BP variability. Real arteries frequently display exponential dependence of P on V with exponent called 'stiffness index'. Expressing BP variability by the standard deviation (SD), a mathematical model shows that the BP variance (SD)² is proportional to the deviation of the average BP from a reference value. The proportionality constant includes both the arterial stiffness at the reference point and the 'stiffness index', both known to depend on age and condition. This result can be shown to predict the well-established linear relationship between repeatedly measured SBP and DBP and expresses the SBP-on-DBP slope by the ratio between systolic to diastolic stiffness. Furthermore, the product (SDsbp – SDdbp) SDdbp is predicted to vary linearly with the pulse pressure (PP). This predicted correlation was tested by applying multi-linear regression to 24h ABP data of 2517 patients (R = 0.53) and the result is presented graphically in Figure B (adjusted to age, SBP-DBP correlation coefficient and PP dipping).

In conclusion, the present model provides testable analytic expressions for the interrelationship between average BP, BP variability and risk-related mechanical properties of an artery.

**PP.38.502 RELATIONSHIP BETWEEN WORK PLACE BLOOD PRESSURE LEVEL AND PSYCHOLOGICAL STATUS IN PATIENTS WITH ARTERIAL HYPERTENSION**

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Results: BPVR (mean ± SE) estimated from Gravity and ambulatory methods were 1.25 ± 0.07 and 1.36 ± 0.04 respectively (p > 0.1). For BPVR restricted to over 0.85 (35 of 40 patients), the same comparison gives 1.34 ± 0.07 vs. 1.37 ± 0.05 (p > 0.06). However, individual BPVRs were weakly correlated (r = 0.32). The SBP-DBP correlation coefficient was better using the Gravity method 0.92 ± 0.03 vs. 0.74 ± 0.01 (p < 0.0001). This difference compensated the effect of over-7-fold smaller number of data points but resulted in a similar average SE of BPVR for individual patients (6.6% vs 4.9%). Age and pulse-pressure dependences were similar in both methods. The Gravity and ambulatory methods provide similar values for restricted BPVR in medicated (1.37 ± 0.08 vs. 1.40 ± 0.06, p > 0.7) and unmedicated patients (1.25 ± 0.13 vs. 1.28 ± 0.08, p > 0.8), BP variability achieved by the Gravity method was comparable to the ambulatory one 10.6/8.2 vs. 13.5/10.0 mmHg (nearly 80%), as was ASI.

Conclusion: Relationship of SBP to DBP variability generated by employing gravity effect at different arm levels during a short clinic visit are similar to prognostically important one obtained during 24 hour ABPM.