P4.03: SUB-ACUTE EFFECTS OF BLOOD PRESSURE LOWERING WITH AMLODIPINE OR LISISNOPRIL ON LOCAL CAROTID ARTERY HAEMODYNAMICS


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Poster Presentation Abstracts

Therapeutic Aspects 1

P4.01 EFFEC T S OF TOCOLYTICAL MEDICATIONS ON THE PERIPHERAL AND CENTRAL HEMODYNAMICS OF HEALTHY FEMALE VOLUNTEERS
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Objective: Atosiban and ritodrine are frequently used tocolytics. Only a few studies investigated the hemodynamic effects of atosiban. We therefore aimed to study the effects on the blood pressure (BP) and BP-amplification.

Methods: Twenty healthy female volunteers (19-41 yrs) were given atosiban (300 µg/min over 2 h) and placebo intravenously (IV) in a random crossover design. Eight of them also received ritodrine IV in escalating doses up to 400µg/min over 2 h. The brachial artery (BA) blood pressures (BP) were taken by an oscillometric device (OMRON 705-IT) and the BP at the common carotid artery (CCA) and the radial artery (RA) were calculated using application tonometry. This was done at the steady state of the highest dose. Statistical analysis was done using Friedman and Wilcoxon test setting value of significance at 0.05.

Results: Effects on atosiban/placebo on N = 20 did not differ from N = 8.

<table>
<thead>
<tr>
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<th>Ritodrine</th>
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<th>p-value</th>
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<tbody>
<tr>
<td>SBP</td>
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SBP (systolic BP), MAP (mean arterial pressure). Friedman-test, * significant vs. atosiban, # significant vs. placebo.

Conclusion: The data show increased SBP at the CCA and BA and lower DBP and MAP under ritodrine. The effects of atosiban did not differ from placebo. Although not statistically significant, the data suggest a nearly absent pressure amplification between CCA-RA during ritodrine administration.

P4.02 EFFEC T S OF TOCOLYTICAL MEDICATION ON BLOOD PRESSURE AND BLOOD PRESSURE AMPLIFICATION
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Objective: Atosiban (oxytocin-antagonist) and ritodrine (β-agonist) are frequently used tocolytics. Only a few studies investigated the hemodynamic effects of atosiban. We therefore aimed to study the effects on the blood pressure (BP) and BP-amplification.

Methods: Twenty healthy female volunteers (19-41 yrs) were given atosiban (300 µg/min over 2 h) and placebo intravenously (IV) in a random crossover design. Eight of them also received ritodrine IV in escalating doses up to 400µg/min over 2 h. The brachial artery (BA) blood pressures (BP) were taken by an oscillometric device (OMRON 705-IT) and the BP at the common carotid artery (CCA) and the radial artery (RA) were calculated using application tonometry. This was done at the steady state of the highest dose. Statistical analysis was done using Friedman and Wilcoxon test setting value of significance at 0.05.

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Conclusion: The data show increased SBP at the CCA and BA and lower DBP and MAP under ritodrine. The effects of atosiban did not differ from placebo. Although not statistically significant, the data suggest a nearly absent pressure amplification between CCA-RA during ritodrine administration.

P4.03 SUB-ACUTE EFFECTS OF BLOOD PRESSURE LOWERING WITH AMLODIPINE OR LISINOPRIL ON LOCAL CAROTID ARTERY HEMODYNAMICS
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2Department of Chemical Engineering, Faculty of Engineering, Imperial College London, London, United Kingdom
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4Pfizer Ltd, Global Research and Development, Sandwich Laboratories, Sandwich, Kent, United Kingdom

Introduction: Anti-hypertensive agents differ in their ability to slow progression of the increase in carotid artery intima-media thickness (IMT) with...
Abstracts
disease and have different effects on the lumen diameter (LD) of the carotid artery. We hypothesised that changes in flow and shear stress in the common carotid artery may contribute to these differences in remodelling.

Methods: 10 treatment naïve hypertensive subjects were recruited into a double blind, placebo controlled, randomised 3-way cross-over study comparing the effects of 7 days treatment with amlopidine or lisinopril. Brachial and carotid blood pressure (BP), common carotid artery (CCA) flow rate, IMT and LD were measured at the end of each treatment period. Magnetic resonance imaging-based computational fluid dynamics was used to calculate time averaged wall shear stress (WSS) in the carotid artery bifurcation.

There were significant reductions in brachial and carotid BP with both active treatments compared to placebo, but brachial and carotid BP did not differ significantly amongst the antihypertensive agents. CCA flow rate was significantly lower and distal vascular resistance was higher following lisinopril treatment compared with amlopidine. WSS on the inner wall of the CCA was significantly lower after lisinopril treatment compared with amlopidine.

Conclusion: Amlopidine causes increased carotid blood flow and increased WSS compared with lisinopril, probably as a result of greater cerebrovascular vasodilatation. These effects could account for differences in arterial remodelling caused by these agents.

P4.04
LONG-TERM REDUCTION IN AORTIC STIFFNESS IN HYPERTENSIVE PATIENTS IS PARTLY INDEPENDENT OF MBP REDUCTION
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Purpose: A decrease in aortic stiffness could theoretically occur after several years of treatment but reduction has never been unequivocally demonstrated in clinical practice. Association with changes in blood pressure remained unclear.

Methods: This longitudinal observational study was conducted in 97 patients (63 1 yrs, 47 women) with treated essential hypertension attending the outpatient hypertension clinic at Pompidou Hospital. Aortic stiffness and carotid pulse pressure (CPP) were determined through carotid-femoral PWV and applanation tonometry. The first measurement of PWV was performed when brachial SBP was lowered below 140 mmHg under treatment. 66 patients had 3 PWV measurements, and 31 patients had 2 measurements during an extended follow-up (5.3 2 yrs).

Results: The reduction in PWV (from 14.2 2.4 to 11.1 2.4 m/s, linear mixed model, P < 0.0001) was associated with a reduction in central SBP (from 132 2 to 122 2 mmHg, P < 0.0001) and central PP (from 59 2 to 54 2, P < 0.001), whereas brachial SBP and PP did not significantly change. In multivariate analysis, the decrease in PWV was significantly associated with age (P < 0.005), duration of follow-up (P < 0.0001), presence of diabetes (P < 0.005) and reduction in brachial MBP (P < 0.005), independently of gender, changes in brachial PP, glomerular filtration rate and hypercholesterolemia.

Conclusion: These results indicate that a large decrease in aortic stiffness (-22%) can be observed in the long term when hypertensive patients were treated under conditions of routine clinical practice. This reduction of aortic stiffness was associated with a reduction in central SBP and PP contrasting with no change in brachial SBP and PP.

P4.05
NONINVASIVE PULSE WAVE ANALYSIS FOR MONITORING THE CARDIOVASCULAR EFFECTS OF NITROMYCETUM DURING LAPAROSCOPIC CHOLECYSTECTOMY
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Aim of Study: Due to absorption of carbon dioxide and elevated intraabdominal pressure, pneumoperitoneum during laparoscopic cholecystectomy has potentially harmful intraoperative cardiovascular effects. Our aim was to test the usefulness of a non-invasive method for detecting these hemodynamic parameters.

Methods: A total of 35 patients, with low anaesthesia risk (ASA 1 and 2) who underwent laparoscopic cholecystectomy were investigated using SphigmoCor arterial wave analyzing system. Conventional pneumoperitoneum was performed, insufflation using carbon dioxide to an intraabdominal pressure of 8-12 mmHg. We determined the estimated central aortic pressure, augmentation pressure and augmentation index, ejection duration and subendocardial viability ratio throughout the surgery. These parameters were recorded after induction of anaesthesia and during the inflation period of surgery.

Results: A significant increase in mean arterial blood pressure (84.5 22.1 vs. 94.0 14.4 mmHg, p = 0.04), aortic pulse pressure (29.5 9.2 vs. 32.7 11.5 mmHg, p = 0.04), augmented pressure (5.9 4.1 vs. 11.0 6.9 mmHg, p < 0.001) and corrugated augmentation index (20.1 13.3 vs. 22.8 12.9, p < 0.001) were recorded after insufflating the abdomen. After deflating the abdomen the measured parameters tended toward normalization.

Conclusion: The derived parameters suggested an increased mechanical cardiac activity and a raised peripheral vascular resistance along with increases in left ventricular end-systolic wall stress. SphigmoCor arterial wave analysis successfully documented hemodynamic changes occurring during laparoscopic surgery. Our results from this non-invasive technique correspond to data reported previously, using invasive hemodynamic monitoring.

P4.06
DIFFERENTIAL EFFECTS OF NEBIVOLOL AND ATENOLOL ON CAROTID ARTERIAL WAVE INTENSITY
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Imperial College London, London, United Kingdom

Background: The hemodynamic effects of the vasodilator β-blocker nebivolol may differ from those of a conventional agent. Wave intensity analysis can describe the energy transported by wavefronts in the arterial system in the direction of wave propagation. A non-invasive ultrasound-based technique [1] was used to compare the effects of nebivolol and atenolol on carotid arterial wave intensity in patients participating in a hypertension treatment study.

Methods: 38 hypertensive patients (age 63 11yrs, 21 female) took part in a double-blind randomised cross-over study. All received bendroflumethiazide 2.5 mg for 6 weeks in advance, and throughout the study. We compared effects of nebivolol 5 mg and atenolol 50 mg on the magnitude of the initial systolic forward compression wave (S), the protodiastolic forward decompression wave (D) (both generated by the heart), the reflected compression wave (C) and local wave speed.

Results: The S and D waves were significantly smaller with atenolol than with nebivolol treatment but wave reflection and wave speed did not differ.

<table>
<thead>
<tr>
<th>Wave parameter</th>
<th>Nebivolol (n = 38)</th>
<th>Atenolol (n = 38)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>S wave, kW m⁻² s⁻¹</td>
<td>735 (586, 1049)</td>
<td>612 (443, 885)</td>
<td>0.007</td>
</tr>
<tr>
<td>D wave, kW m⁻² s⁻¹</td>
<td>220 (183, 284)</td>
<td>164 (106, 225)</td>
<td>0.001</td>
</tr>
<tr>
<td>C wave, kW m⁻² s⁻¹</td>
<td>122 (74, 168)</td>
<td>97 (76, 150)</td>
<td>0.4</td>
</tr>
<tr>
<td>Wave speed, m s⁻¹</td>
<td>6.67 (5.70, 9.28)</td>
<td>6.61 (5.22, 8.40)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Medians (25th, 75th percentiles), * Wilcoxon’s signed rank test

Conclusions: In hypertensive patients nebivolol has a more favourable effect than atenolol on left ventricular wave generation without increasing wave reflection.


P4.07
INFLUENCE OF LONG-ACTING ISOSORBIDE-5-MONONITRATE ADMINISTRATION ON LARGE ARTERIAL STIFFNESS IN PATIENTS WITH ESSENTIAL HYPERTENSION
Cardiology Research Center, Moscow, Russian Federation

AIM of this study was to evaluate the clinical efficacy of long-acting nitrates, isosorbide-5-mononitrte (ISMN), in addition to ACE inhibitor on artery stiffness in patients with essential hypertension.

METHODS: 40 hypertensive patients (mean age 61.3 7.4 years, 9 male, 31 female, mean SBP/DBP = 158.1 17.9/91.7 7.9 mmHg) received moexipril in individual titrated doses (mean dose 11.7 4.8 mg daily) for 3 months. 20 patients, which retained SBP > 140 and/or DBP > 90 mmHg, received additional ISMN (50 mg daily) for 4 weeks. Other patients formed the control