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# 11. THE EFFECT OF LONG-TERM ADMINISTRATION OF HYDROCHLOROTHIAZIDE ON CENTRAL BLOOD PRESSURE

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the potential role of NO and caveolin-1, we examined the plasma activity of NOx, eNOS, phosphorylated-eNOS and expression of caveolin-1. The relaxation in response to acetylcholine was significantly enhanced in ROS compared to CON. Expression of eNOS RNA was unchanged, whereas NOx level and phosphorylated-eNOS at serine-1177 was increased accompanied with depressed level of caveolin-1 in ROS.

We conclude that HMG-CoA reductase inhibitor can improve impaired endothelial dysfunction in SHR, and its underlying mechanisms are associated with increased NO production. Furthermore, HMG-CoA reductase inhibitor can activate the eNOS by phosphorylation related to decreased caveolin-1 abundance. These results imply the therapeutic strategies for the high blood pressure-associated endothelial dysfunction through modifying caveolin status.

#### 10. THE USEFULNESS OF ESTIMATED CAROTID SYSTOLIC BLOOD PRESSURE USING FORM PWV/ABI IN BLOOD PRESSURE LOWERING THERAPY

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**Background:** Central systolic blood pressure (central-SBP) can be estimated noninvasively and antihypertensive drugs may exert different effects on central-SBP. We investigated the usefulness of carotid systolic blood pressure (carotid-SBP) estimated by form PWV/ABI in blood pressure lowering therapy.

**Methods:** We evaluated pulse wave velocity, carotid augmentation index (AI), carotid-SBP in 329 patients (301 hypertensives, 172 men,  $65 \pm 12$  years old) using form PWV/ABI. Antihypertensive drugs were evaluated in those patients.

**Results:** Mean brachial blood pressure (b-SBP) was  $136 \pm 21$  mmHg and carotid-SBP was  $147 \pm 25$  mmHg. We determined delta-SBP as carotid-SBP - b-SBP, and we divided the subjects into group A (delta-SBP  $< 0$  mmHg) and group B (delta-SBP  $> 0$  mmHg). The number of group A was 22 patients and that of group B was 307 patients. There were no differences of mean age between these two groups. Although b-SBP of group A ( $137 \pm 21$  mmHg) was similar to that of group B ( $136 \pm 21$  mmHg), b-diastolic BP of group A ( $83 \pm 12$  mmHg) was different from that of group B ( $77 \pm 13$  mmHg,  $p = 0.0456$ ). Carotid AI of group A ( $13 \pm 14\%$ ) is lower than that of group B ( $23 \pm 18\%$ ,  $p = 0.0160$ ). The evaluation of the effect of antihypertensive agents showed that Ca antagonists, angiotensin receptor blockers, angiotensin converting enzyme inhibitors and diuretics did not affect delta-SBP significantly. However, those who had  $\beta$  blockers or blockers showed higher delta-SBP compared to those who without these drugs.

**Conclusion:** Estimation of carotid-SBP using form PWV/ABI is useful for the evaluation of the effects of antihypertensive drugs on brachial and central BPs.

#### 11. THE EFFECT OF LONG-TERM ADMINISTRATION OF HYDROCHLOROTHIAZIDE ON CENTRAL BLOOD PRESSURE

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**Background:** It's unknown whether there is much benefit on central aortic pressure than brachial pressure while long-term administration of hydrochlorothiazide in patients with essential hypertension.

**Methods:** The retrograde analysis was conducted at three of the participating centers in the Felodipine Event Reduction (FEVER) study. 76 of 129 patients in placebo group, who kept hydrochlorothiazide monotherapy over 36 months period, and took pulse wave recording at randomization, 12 month, 24 month and 36 month, were included into the final analysis. Radial artery pressure waveforms were measured with applanation tonometry, and convolved into the ascending aortic pressure waveforms, using the FDA-approved SphygmoCor system. The analysed parameters in aortic pressure waveform included first peak pressure, secondary peak pressure, diastolic pressure, pulse pressure, augmentation and augmentation index.

**Results:** In comparison with baseline, there were substantial falls ( $P < 0.001$ ) in brachial SP/DP and in central aortic SP/DP with no difference, slight falls ( $P < 0.05$ ) in aortic augmentation, and no significant falls ( $P > 0.05$ ) in augmentation index and heart rate.

**Conclusion:** Long-term administration of hydrochlorothiazide resulted in the similar reduction of both brachial pressure and central aortic pressure without the change of augmentation index, which could exclude definite benefit on central aortic pressure than brachial pressure.

#### 12. THE EFFECT OF ORALLY SINGLE DOSE OF SLOW-RELEASE ISOSORBIDE-5-MONONITRATE ON CENTRAL BLOOD PRESSURE IN HEALTHY VOLUNTEERS

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**Background:** The cuff sphygmomanometer failed to show consistent alteration in brachial blood pressure with slow-release isosorbide-5-mononitrate (IS-5-MN), even though the drug proved very effective in relieving angina pectoris. So far, the effect of orally single dose of slow-release isosorbide-5-mononitrate on central blood pressure is not known.

**Methods:** Using self-control study before and after treatment in a total of 22 healthy volunteers, the effects of slow-release IS-5-MN 60 mg in single dose form were assessed over a twenty four hour period through analysis of the radial pulse waveform, calibrated against conventional cuff sphygmomanometry. Ascending aortic pressure waveforms were generated from the radial waves, using a validated generalised transfer function. The concentration of 5-ISMN were measured by HPLC-MS.

**Results:** After taken the drug, the concentration of 5-ISMN was rapidly increased to peak at 4 h, then linearly decreased to 187.6 ng/ml at 24 h. There was no consistent change in heart rate or brachial pressures except for a decrease in systolic pressures and a increase in heart rate ( $p < 0.01$ ) at 2-6 hour. In contrast, there were substantial and significant decreases in aortic systolic pressures, augmented pressures, augmentation index and ejection duration ( $p < 0.001$ ) at 0.5 h-16 h.

**Conclusion:** Pulse waveform analysis exposes concentration dependent effects of 5-ISMN on the aortic waveform, suggesting muscular conduit arterial dilatation with reduced wave reflection and venous dilatation with reduced ejection duration at the low and intermediate concentration, arteriolar dilatation and decreased peripheral resistance at the high concentration.

#### 13. THE LONG-TERM EFFECT BETWEEN CO-ADMINISTRATION OF SIMVASTATIN AND EZETIMIBE AND ATORVASTATIN ON CENTRAL PULSE WAVE VELOCITY IN ADULTS WITH HYPERCHOLESTEROLEMIA

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**Background:** The various statin might contribute to a change in arterial stiffness independent of the cholesterol-lowering effects of statin therapy. The aim of this study was to compare the short-term effect between co-administration of simvastatin and ezetimibe (vytorin) and atorvastatin (lipitor) on pulse wave velocity (PWV).

**Methods:** We enrolled 27 patients with hypercholesterolemia (Total cholesterol  $> 200$  mg/dL). The patients were randomly divided into two groups according to statin (vytorin: 13 patients, lipitor: 14 patients). They were treated vytorin 10/20 mg and Lipitor 20 mg for 1 month, then vytorin 10/10 mg and Lipitor 10 mg for 5 months. We measured the carotid-femoral PWV (cfPWV), and lipid profile at baseline, 1 month, and 6 months after treatment with the statin.

**Results:** The total cholesterol and LDL levels in both groups were significantly decreased 1 month later, and they were slightly increased 6 months later. In addition, the change of total cholesterol was not different in both groups. The central PWV (cfPWV) in lipitor group was significantly decreased compared with those in vytorin group after 6 months ( $-0.61 \pm 1.23$ ,  $0.24 \pm 1.24$  m/sec, respectively).

**Conclusion:** Although co-administration of simvastatin and ezetimibe for 6 months might show similar lipid lowering effect compared with atorvastatin, only atorvastatin might show pleiotrophic effect for long-term treatment in hypercholesterolemia.

#### 14. USING CENTRAL BLOOD PRESSURE TO GUIDE THERAPY IN HYPERTENSION: BP GUIDE STUDY DESIGN AND INITIAL FINDINGS

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**Background:** Estimated central blood pressure (BP) predicts cardiovascular mortality independent of brachial BP, but whether central BP may be useful in